Special Report Series, No. 21.

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MEDICAL RESEARCH COMMITTEE

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THE DIAGNOSTIC VALUE OF THE WASSERMANN TEST

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ERRATA.

Page 41. *Heading*. *For* 25 *read* 30.

Page 47. *Last two lines of* § (*1*). *For* (McIntosh—(Suspicious), Browning—). *read* (McIntosh—, Browning—(Suspicious)).

Page 48. *Line* 7. *For* "positive incomplete" *read* "Negative."

(20989) 700.

MEDICAL RESEARCH COMMITTEE

REPORTS

OF THE

SPECIAL COMMITTEE UPON THE STANDARDIZATION OF PATHOLOGICAL METHODS

No. 4.—THE DIAGNOSTIC VALUE OF THE COMPLEMENT FIXATION TEST IN SYPHILIS, COMMONLY KNOWN AS THE WASSERMANN TEST

Approved for publication by the Medical Research Committee,
7th June, 1918.

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(*Secretary*).

In April, 1917, the Medical Research Committee invited the following special Committee to consider how far it may be practicable and desirable to obtain the standardization of routine pathological methods, and to report to them. The special Committee were empowered to co-opt additional members for particular divisions of their subject.

COLONEL J. G. ADAMI, M.D., F.R.S., C.A.M.C. (*Chairman*).
MAJOR F. W. ANDREWES, M.D., F.R.S., R.A.M.C., T.
PROFESSOR WILLIAM BULLOCH, M.D., F.R.S.
CAPTAIN S. R. DOUGLAS, I.M.S. (*Secretary*).

For the consideration of the subjects dealt with in the Report now presented the Special Committee invited the co-operation of COLONEL L. W. HARRISON, D.S.O., K.H.P., who by permission joined the Committee for this purpose.

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REPORTS
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SPECIAL COMMITTEE UPON THE STANDARDIZATION OF PATHOLOGICAL METHODS

No. 4.—THE DIAGNOSTIC VALUE OF THE COMPLEMENT FIXATION TEST IN SYPHILIS, COMMONLY KNOWN AS THE WASSERMANN TEST

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In their previous interim Report upon the Wassermann Test (No. 1 in the present Series) the Committee expressed the opinion that 'there is no process of biochemical diagnosis that gives more trustworthy information or is liable to a smaller margin of error than the Wassermann test when it is performed with completeness and with proper skill and care'.

From time to time instances have been brought to the notice of the Committee in which serious discrepancies have been observed in the results of Wassermann tests made successively upon sera from the same case or simultaneously upon two or more portions of the same serum by different observers. Reported discrepancies are familiar of course to many. Where discrepancy is found the Committee believe that it may almost always be traced to want of experience or skill in the observer or to some failure to perform the test with full completeness. In some instances within their recent knowledge, however, discrepancies have been reported which could not be easily assigned, or so it was alleged, to any of these possible causes of error. It appeared desirable accordingly to the Committee to arrange a definite trial in which a series of specimens from patients whose clinical history was known, should be examined by skilled observers of recognized experience, using similar fractions of serum in each case, and employing the original Wassermann test with its full controls.

Dr. J. H. Sequeira of the London Hospital was good enough to offer his co-operation, and undertook to select from among his patients a series of about 100, to include not only treated or untreated cases in which in his opinion syphilitic infection was or had been undoubtedly present, but also those in which his clinical diagnosis was dubious. He was also requested to bring within the series some cases of non-syphilitic disease for additional purposes of control. While Dr. Sequeira retained his own full clinical notes of all the patients in the series, he arranged to divide the serum drawn from each into three parts, and to send these three similar fractions, labelled only with appropriate numbers, to three observers invited by the Committee to perform the tests. Colonel L. W. Harrison, Dr. Carl Browning, and Dr. James McIntosh kindly undertook to determine the Wassermann reaction in the specimens provided under these conditions, each worker employing the full method previously described in association with his name in the interim report of the Committee already published. Medical Research Committee, The Wassermann Test, 1918. Special Report Series, No. 14.

In addition, the series of sera was tested by Dr. Robert Donald (London Hospital) by means of his drop-technique,[1] which in this instance was a careful copy on a $\frac{1}{10}$ scale of the method of Fildes and McIntosh. Dr. Donald's results appear in the column under his name in Table XIV.

In due course reports upon the tests performed by these pathologists, indexed under the reference numbers attached to the sera, were sent to the Secretary of the Medical Research Committee, who had received from Dr. Sequeira the clinical details and his diagnosis of every case given under the corresponding numbers. The results were then collated and are set out below in this report. Dr. Sequeira has also given his own analysis of the results as communicated to him.

The Committee would desire to express their grateful acknowledgements to Dr. Sequeira for the time and labour he has been willing to give to the inquiry, and to the four pathologists who have so generously submitted their work to this open test. The Committee are confident that many others will share with them the sense of obligation under which they have been placed.

By way of introduction to the report now submitted upon the outcome of this trial, the Committee have given a historical survey of the Wassermann reaction, and of the chief publications which have already been made with reference to its diagnostic value.

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[1] *Lancet*, 1912, I, 1752; *Proc. Royal Soc.*, 1913, 76 B, 202; *Lancet*, 1915, II, 1243, and *Lancet*, 1916, II, 423.

I. HISTORICAL SURVEY

The history of the so-called Wassermann reaction can be traced back to the discovery of the Bordet-Gengou phenomenon in 1901. These investigators found that when certain antibodies were mixed *in vitro* with their antigens and with complement a reaction of some kind took place whereby the complement disappeared from the mixture. This was shown by the fact that when another antigen, composed of red blood corpuscles, and its homologous amboceptor, were added to the mixture no haemolysis ensued. The complement was described as being 'fixed'. If the first serum did not contain the necessary antibody the complement remained in the mixture, so that the subsequent addition of suitably sensitised red blood corpuscles led to haemolysis. In this way Bordet and Gengou showed that the reaction was specific, and that the method could be utilized for determining whether an antibody was present in a given serum or not. In 1906 Wassermann, in conjunction with Neisser and Bruck, showed that the principle of Bordet and Gengou was applicable to the diagnosis of syphilis, and from this time onward the phenomenon appears in the literature as 'Wassermann's reaction'. Wassermann and his collaborators used as an antigen the extract of the liver from cases of congenital syphilis. Improvements and modifications, however, rapidly took place as the result of researches by Marie and Levaditi, Landsteiner, Müller and Pötzl, Porges and Meier, Levaditi and Yamanouchi, Sachs, Browning, Cruickshank and Mackenzie, Thomsen and Boas, Noguchi, Fildes and McIntosh, and others. The admirable book of Boas also had a great influence in raising the whole standard of the technique. The Wassermann test began to be practised on a truly gigantic scale all over the world, and rapidly took its place as an important adjunct in the diagnosis of syphilis.

It was very early recognized that in cases of undoubted syphilis the reaction is positive in a large percentage of cases. Already in 1910 Wassermann (5) asserted that with his co-workers he had carried out more than 10,000 examinations and 'we have never yet made a false diagnosis'. Without at present accepting this statement at its face value, and assuming that all serologists are alike competent and trustworthy, it may be pointed out that the diagnostic value of a test like the Wassermann reaction depends largely on the frequency with which a positive reaction is found to occur in undoubted examples of the disease. If the incidence of positive results in these circumstances is an exceedingly high percentage a negative result may possess undoubted significance. It is now a universal experience that positive results occur so frequently in the acute stages of syphilis that a clinical diagnosis which does not coincide requires reconsideration and, if necessary, revision. It is likewise certain that even in the hands of the most skilled serologists a negative result may be met with even in secondary syphilis, and still more is this the case in the tertiary and latent forms of the disease. A negative reaction, especially if obtained on one occasion, cannot therefore exclude syphilis.

The reputation of the Wassermann test depends on three factors, the serological technique, the serologist himself, and the accuracy of the clinician on whose diagnosis the results of the serologist are judged. But we know that all of these factors are fallible, and thus it is useless to attempt to gauge the value of the test merely by taking all the published series of figures and calculating what appears to be the percentage of correct diagnoses. It is often assumed that a test like the Wassermann reaction can be judged by the frequency with which it satisfies clinical diagnoses; but, in general, clinical diagnosis is a comparative estimate of probabilities, and its nature is such that the ripe experience of years may be reversed by an accurate scientific method. This is clearly manifest when an analysis of Wassermann tests is made. The agreement with clinical demands is least when sera are sent by a number of clinicians of varied knowledge and experience to be tested, and when the accuracy of the diagnosis cannot be called in question. When, on the other hand, the diagnoses are made after careful consideration, and on the basis of a wide and special experience, and when the diagnoses, if necessary, are reconsidered after further investigation of the case along lines suggested by the serological result, it is found that the test possesses an unusually high degree of specificity.

It is hardly necessary to point out that the ultimate value of the Wassermann test can only be determined by submitting a series of cases to complete examination, and this would include not only the clinical opinion, however accurate this may be, but also the demonstration of Spironema pallidum where possible, and the pathological anatomical study of material obtained either during life or after death. In spite of the immense number of Wassermann tests which have been performed, the neglect of such precautions has deprived many of them of much of their value. Thus equally positive assertions are made both for and against the test, and as the matter is one of paramount practical importance, it is essential that some definite opinion should be arrived at if possible. As far as we have been able to ascertain, the literature contains no case series of any magnitude in which every precaution, clinical, serological and anatomical, has been taken to establish the diagnosis with certainty. In the majority, the value of the Wassermann test has been judged by the exactitude with which clinical demands are satisfied. On account of the modifications and improvements in technique, it is justifiable to make some selection of the published results, and it seems fair to separate these results into two great series, those published before and those after the appearance of Boas's book in 1911.

Boas (12) has collected the data from the older literature, and has summarized them as follows:

	Total no. of Cases	*Positive Reaction*	*% of Positive Reactions*
Primary syphilis	1060	629	59 %
Secondary syphilis	3526	3181	90
Tertiary syphilis	1212	1020	84·1
Latent syphilis, early	983	504	51
,, ,, late	1520	605	39
Tabes dorsalis	159	115	72
General paralysis of insane	405	402	99·2

It is thus apparent that in a high percentage of cases of active syphilis the Wassermann reaction is positive. It is equally a fact that in the great majority of diseases which are non-syphilitic the reaction is negative. With improvements in technique the idea has gained ground more and more that with exceedingly few exceptions the reaction is specific for syphilis. While the early publications showed a high percentage of positive reactions in syphilis, the later researches have shown this to be more than could have been suspected. Thus Boas himself has published a careful series of 6043 sera which he tested, with the following results:

Nature of Condition		*Total no. of Cases*	*Positive Reaction*	*Negative Reaction*
Primary syphilis		137	99	38
Secondary syphilis	total cases	747	729	18
	untreated	437	437	0
	recurrences after treatment	310	292	18
Tertiary syphilis	total cases	167	155	12
	not previously treated	132	129	3
	previously treated	35	26	9
Latent syphilis	less than three years after infection	363	143	220
	more ,, ,, ,,	185	87	98
Tabes dorsalis	total cases	58	40	18
	untreated cases	25	25	0
	treated cases	33	15	18
Dementia paralytica	blood serum	243	243	0
	cerebro-spinal fluid	201	189	12
Congenital syphilis	manifest	121	121	0
	latent	34	28	6
Congenital weakmindedness		2061	31	2030
Control cases		1927	5	1922
		6043		

Boas's series of 1927 control sera was obtained from individuals either normal or suffering from one or other of nearly 100 different affections regarded as non-syphilitic. In this large series he encountered a positive Wassermann reaction only 5 times. Of these 5 positive reactions, 1 was a case of leprosy, 1 of scarlatina (of 73 examined), and 3 of narcotised patients (of 60 examined).

In this country Bassett Smith, Fildes and McIntosh, L. W. Harrison and Browning and Mackenzie have published series of results which in the main confirm those of Boas. Thus Bassett Smith (1) (1910) analysed 1116 blood reactions with the following results:

	Total no. of Cases	*Positive Reactions*	*Negative Reactions*	*% of Positive Reactions*
Primary syphilis	183	139	44	75·9 %
Secondary syphilis (early)	407	384	23	94·3
Secondary (late) and tertiary syphilis	51	48	3	94
Congenital syphilis	1	1	0	100
Latent syphilis	39	18	21	46
Tabes and general paralysis	20	18	2	90
Chancroids	280	0	280	0
Gonorrhoea	39	0	39	0
Other diseases	146	2	144	1·3

Of the 2 cases among the non-syphilitic which reacted positively one was a case of scarlet fever, the other malignant disease of the liver with great jaundice. In a later publication (1916) Bassett Smith (24) gives his final results as follows:

	Positive		*Negative*
Primary syphilis	74 %	Chancroids	100 %
Secondary syphilis	93	Gonorrhoea	100
Tertiary syphilis	89	Other diseases	97
Parasyphilis	90		

The other diseases which gave positive results were acute malaria, scarlet fever, trypanosomiasis, and kala-azar.

In a series of 489 sera from syphilitic soldiers L. W. Harrison (4) (1910) obtained the following results:

Primary	71·8 %	positive
Secondary	90	,,
Tertiary	83·5	,,
Early latent	56·6	,,

Browning and Mackenzie (6) (1911) published the results on 101 cases from a wide variety of acute and chronic diseases where syphilis could in all probability be excluded. Only 1 gave a + reaction. It was a case diagnosed clinically as chronic phthisis: no tubercle bacilli could, however, be found in the sputum. The various conditions were classed as follows:

Acute tuberculosis	6
Chronic tuberculosis	5
Malignant disease	5
Lobar pneumonia	4
Bronchopneumonia	3
Enteric fever	14
Typhus fever	14
Scarlet fever (various stages)	37
Cerebro-spinal meningitis	3
Eclampsia	4
Surgical cases	6

In an elaborate paper on the Wassermann reaction and its application to neurology, Fildes and McIntosh (7) published the results obtained on 372 cases which, unknown to them, were diagnosed as 'clinically certain' syphilis by Dr. J. H. Sequeira, Dermatologist to the London Hospital. Their results appear to show that with an improved technique the specificity of the Wassermann reaction is almost absolute in cases of syphilis.

	No. of Cases	*Positive W. R.*	*Negative W. R.*	*% of Positive Reactions*
Primary syphilis	33	31	2	93·9 %
Secondary syphilis	109	108	1	99
Tertiary syphilis	195	190	5	97
Congenital syphilis	35	35	0	100
	372	364	8	97·8

In 1913 the well-known serologist, Rudolf Müller (9), assistant for years in the Serodiagnostic department of Finger's great institute for syphilology and dermatology in Vienna, published a *résumé* of the results he had obtained in the examination of sera from 70,000 patients. From these results the following figures have been extracted. These are of importance not only from their number, but also from the fact that the examinations were carried out by one well qualified for the task.

In over 2000 healthy persons in whom every possible care was taken to eliminate syphilis, only 1 gave a positive Wassermann reaction. Müller believed that this solitary instance was one of latent syphilis that had escaped detection.

In 5000 cases of diverse diseases other than syphilis, and mostly severe in character, 220 = 4·4 % gave an incomplete positive reaction. In 100 of these, however, subsequent examination indicated evidence or suspicion of syphilis, leaving 120 cases (*ca.* 2·4 %) unaccounted for. In diseases other than syphilis Müller found complete positive reactions only in certain protozoal infections and in leprosy.

Passing to undoubted syphilitic cases his results were as follows:

Primary syphilis, 1320 cases, comprising		
Complete positive reactions	500	58·1 %
Incomplete positive reactions	280	
Negative reactions	540	41·9 %
Secondary syphilis, 3500 cases, comprising		
Complete positive reactions	3300	= 94·3 %
Medium to almost complete positive reactions	125	= 3·6 %
Slightly positive reactions	53	= 1·5 %
Negative reactions	22	= 0·6 %
Tertiary syphilis, 510 cases		
Complete positive reactions	482	= 94·5 %
Medium to almost complete positive reactions	20	= 3·9 %
Slight positive reactions	5	= 1·0 %
Negative reactions	3	= 0·6 %

Among these tertiary lesions there were 468 cases of tabes dorsalis, of which 284 (60·7 %) gave a complete positive reaction, and 386 instances of general paralysis of the insane with 376 (97·4 %) complete positive reactions.

Latent syphilis, 11,500 cases, with the following results:

	No. of Cases	*Complete positive W. R.*	*Incomplete positive W. R.*	*Negative W. R.*
Latent syphilis	11500	2780 (24·1 %)	2520 (21·9 %)	6200 (54 %)
Early latent syphilis	4600	2180 (47·4 %)	980 (21·3 %)	1440 (31·3 %)
Late latent syphilis	4800	864 (18 %)	816 (17 %)	3120 (65 %)

Working in the laboratory of the Army Medical School, Washington, D.C., Craig (17) has published (1915) the analysis of 18,000 Wassermann tests made by himself. His experience has been much the same as that of the authors just quoted. Among 2643 individuals either normal or suffering from diseases other than syphilis, positive Wassermann reactions were found only 11 times (0·4 per cent.). In 4 cases the diagnosis was malaria, in 3 tuberculosis, although 2 of these ultimately give a clinical history of syphilis; in 3 the diagnosis was pityriasis rosea, and in the remaining case a diagnosis was not established at all. A single Wassermann test on each of 4658 cases diagnosed as syphilis yielded the following results:

	Total Cases	*Positive W. R.*	*Negative W. R.*	*% of Positive W. R.*
Primary	908	813	95	89·5 %
Secondary	1889	1817	72	96·1
Tertiary	638	558	80	87·4
Latent	1173	790	383	67·3
Congenital	28	25	3	89·2
Parasyphilis	22	15	7	68·1
	4658	4018	640	86·2

From his experience Craig concluded that if the diseases other than syphilis which occasionally give a positive Wassermann reaction can be excluded, a 'double plus' (+ + = absolute inhibition of haemolysis) is diagnostic of syphilis, and the reaction is absolutely specific whether symptoms are present or not, and whether there is or is not a history of syphilis. Under the same conditions a 'plus reaction' (+ = at least 50 % of haemolysis) may in primary, tertiary, or latent infections be interpreted as diagnostic, provided there is a clear history of infection or the presence of clinical symptoms. In the absence of either history or suspicious symptoms a + reaction should never be considered as diagnostic.

A diagnosis of syphilis should never be made on a 'plus-minus' reaction (± = less than 50 per cent. of haemolysis). Many normal individuals give such a reaction, and it is of no value whatever as a diagnostic sign of syphilis.

Craig also considers that a single negative reaction (−) is of no value in excluding syphilis. Even the most severe secondary cases occasionally give such a reaction. It is only when a negative reaction is repeatedly obtained over a long period that it can be considered as good evidence of the disappearance of the disease, and in all such cases the result of the test upon the cerebro-spinal fluid, a luetin test and a provocative Wassermann test should be made if one desires to be sure of the absence of syphilis.

Buhman (27) (1916) examined 288 cases in which there was no evidence of syphilis. They were classified in three groups: 1. skin diseases, 2. tumours, 3. miscellaneous.

		No.	*Negative*	*Positive*
GROUP I.	Pityriasis rosea	8	8	0
	Scabies	15	15	0
	Dermatitis	5	5	0
	Eczema	25	25	0
		53	53	0

		No.	Negative	Positive	Weak Positive
GROUP 2.	Sarcoma	12	12	0	0
	Malignant adenoma	15	15	0	0
	Glioma of brain	2	2	0	0
	Carcinoma	107	96	9	2
		136	125	9	2

		No.	Negative	Positive
GROUP 3.	Trichinosis	3	3	0
	Pernicious anaemia	4	4	0
	Hodgkin's disease	3	3	0
	Sporotrichosis	3	3	0
	Scarlet fever	15	15	0
	Lepra	6	3	3
	Tubercle	35	33	2*
	Malaria	10	10	0
	Arthritis	6	6	0
	Meningitis	10	10	0
	Streptococcal infections	4	4	0
		99	94	5

* These two positive cases ultimately gave a definite history of syphilis.

All these figures show that in the hands of trustworthy workers *a positive reaction is indicative of syphilis with exceedingly few exceptions.* The well-known fact that there may be no symptoms of syphilis in undoubted instances of the disease while the Wassermann reaction is positive is a point of great importance in estimating the value of the reaction. It also explains why a certain number of positive reactions may be obtained either in persons believed to be normal or suffering from conditions other than syphilis. Examinations of cases like these have been utilized to determine the incidence of syphilis in the general population. Such determinations are fallacious in that the 'population' is not general, but selected—usually a hospital population. Thus Fildes (29) performed 1002 Wassermann tests on persons of nineteen years and upwards, who visited the London Hospital for reasons wholly unconnected with syphilis. These reasons were fractures, wounds, diseases of teeth, cancer, hernia, and varicose veins. All medical diseases were excluded. In certain of the cases which yielded a positive reaction Fildes attempted to extract an admission of syphilis, but ultimately found that the inquiry was resented. In the first eight cases giving a positive reaction there was, however, a definite history of syphilis in three. One denied syphilis, and the remaining four were not seen a second time after the specimen of blood had been examined. Fildes' results showed that out of 1002 sera tested 84 were positive = 8·3 per cent. The series was composed of 616 males with 64 positive = 10·3 per cent., and 386 females with 20 positive = 5·1 per cent. If from the London Hospital 'population' 197 aliens with 13 positives be excluded, there remain 805 British cases with 71 positive results = 8·8 per cent. Grouping the cases in decennial age groups, and on the assumption of the specificity of the Wassermann reaction, Professor Karl Pearson, who analysed the figures, concluded that in the particular population examined 8 to 12 per cent. of the males, and 3 to 7 per cent. of females had syphilis. In Fildes' series no general attempt was made to elicit a history of syphilis. Bruhns (25) (1916) in Charlottenburg (Berlin) has examined 1800 cases of patients attending a skin-disease hospital. All were investigated for a history or for signs of syphilis, and the cases were chosen where this could so far as possible be excluded. His results were as follows:

	Males		Females	
Age	*No. of Cases examined*	*No. of Syphilitics*	*No. of Cases examined*	*No. of Syphilitics*
16–20	308	1	145	9
21–30	603	4	313	39
31–40	245	9	64	11
41–50	48	3	26	4
over 50	30	1	18	2
	1234	18 = 1·5 %	566	65 = 11·5 %

Of the 18 males 12 had no other sign but a + W. R., while 6 had some other suspicious sign. In 6 there was a history of a sore which had been alleged not to be syphilitic. Of the 566 females a number were of the lower and prostitute class. In 132 women and girls where there was no suspicion only 2 = 1·5 % reacted positively.

It has been asserted by some writers that a single Wassermann test is not of value, and should not be used as a basis for the diagnosis of the disease. The value of 'first diagnostic Wassermann tests' has been made the subject of inquiry for the purposes of this report by Staff Surgeons P. Fildes and R. J. G. Parnell on 1414 men admitted to the Royal Naval Hospital, Haslar, for syphilis or suspected syphilis.

The material was unselected, every man being included who was admitted between certain dates (except a few who by mistake were not tested or were otherwise unsuitable).

The cases were admitted in all stages of treatment. They were not fresh untreated cases, such as are usually met with in a civil hospital. There was a preponderance of early cases.

Of the 1414 men 1157 (81·8 per cent.) gave positive reactions, and 257 (18·1 per cent.) negative.

The evidence of syphilis in the positive cases was as follows:

a. 938 men were conclusively shown to be syphilitic by reason of the presence of S. pallidum or clinical signs or histories of a generalized condition characteristic of syphilis.

b. 62 men were accepted as syphilitic on the evidence of anti-syphilitic treatment having been applied previously for local lesions which in the opinion of the medical officer responsible for treatment were syphilitic.

c. 16 were shown to be syphilitic by means of lumbar puncture and ophthalmological examination.

d. 5 were shown to be syphilitic by methods *b* and *c* combined.

e. 61 were accepted as syphilitic by reason of previous or subsequent positive Wassermann reactions.

f. 4 men were diagnosed by methods *c* and *e*.

g. 3 men were diagnosed by methods *b* and *e*.
h. 3 men were diagnosed by methods *b*, *c*, and *e*.
i. 65 men remained with positive reactions, but no direct evidence of syphilis was obtainable. Practically all were suffering from venereal conditions.

The evidence of syphilis in cases giving a negative Wassermann reaction was:

a. 127 men had sores in which S. pallidum was found.
b. 34 men had no lesions, but S. pallidum had been found in sores now healing or recently healed.
c. 5 men had sores in which S. pallidum could not be found, but they nevertheless developed syphilis.
d. 1 man had manifest secondary syphilis.
e. 2 men had manifest tertiary syphilis.
f. 2 men had cerebro-spinal syphilis.
g. 10 men had no lesions, but more or less undoubted histories of syphilis.

In the remaining 76 cases there was no evidence of syphilis. They included the following groups:

23 men had sores which were untreated, and yet they did not develop syphilis.
45 men had sores in which S. pallidum could not be found. They were untreated, but did not come again under examination.
2 men were said to have had syphilis, but there was no evidence of this.
6 men had been diagnosed as syphilis on insufficient grounds by outside practitioners.

With regard to the incidence of positive Wassermann reactions in different periods of the disease the following figures were made out. Of a total of 1338 cases of syphilis

166 were in the primary stage before the W. R. had become positive.
446 primary cases (= 72·7 per cent.) gave a positive W. R., but there were no other signs or history of general infection except glandular enlargement up to and including 18 months from infection.
463 cases of syphilis with signs or history of general infection up to and including 18 months from infection. This group included chiefly early secondary, but also some latent and early tertiary cases. One of the secondary cases gave a negative reaction. In this group the percentage of positive reactions was therefore 99·7 per cent..
263 cases of late secondary, tertiary, or latent syphilis over 18 months from infection. Of these, 2 cases of tertiary, 2 cases of cerebro-spinal, and 10 cases of 'latent' (possibly cured) syphilis gave negative reactions, making a total of 94·7 per cent. of positive reactions in this group.

These results show that a single Wassermann test under the conditions stated possesses a high diagnostic value.

A usual procedure of determining the accuracy of a clinical method of diagnosis is to verify such a diagnosis by post-mortem examination. It is a matter for surprise that, in spite of the fact that vast numbers of sera have been examined for the Wassermann reaction during life, there exist but few series of published cases where the results of Wassermann findings have been analysed in the light of a subsequent autopsy carefully carried out. With a view to obtaining some knowledge on this highly important side of the question, Dr. H. M. Turnbull, Pathologist to the London Hospital, undertook to analyse his post-mortem records, and has communicated the results to the Committee. These results, which will subsequently be published in detail, concern especially the value of the Wassermann reaction in sera obtained after death. There occur, however, a number of cases in which the Wassermann test was carried out during life in patients who subsequently died, and were subjected to post-mortem examination. We have selected one such series of cases in which the test was made with heart-cholesterin antigen, as described by Fildes and McIntosh, who actually carried out the examination of the sera. No selection of the cases was made, the list including all the examinations of the kind made in the London Hospital up to 1916. The autopsies were carried out by Dr. Turnbull as completely as possible, and numbered 98, of which 54 comprised the body only, while the remaining 44 comprised complete examinations of body and head.

Without at present including all the details accumulated by Dr. Turnbull, it suffices to state that his ultimate conclusion was that there was no proof that the test was inaccurate in 94 out of these 98; in 88 indeed the post-mortem result and the Wassermann test were in complete agreement, both being negative 60 times and both positive 28 times.

In 6 cases syphilitic lesions were not detected, although the serum gave a positive reaction. The presence of a syphilitic infection could however not be excluded. In 1 case, an infant, the histological evidence 'appeared to have excluded a syphilitic infection'; the parents were proved to be syphilitic.

There remain therefore only 3 cases out of the 98 in which the autopsy threw doubt on the accuracy of the test. In 1 case the Wassermann reaction was negative in the serum (2 ante-mortem and 1 post-mortem tests) in the presence of a lesion of the spinal meninges and cord, which was in all probability syphilitic and apparently still active. In the second case the reaction was negative in the serum in the presence of three lesions, one syphilitic (aortitis), one probably syphilitic (glossitis), and the other possibly syphilitic (fibrosis of testicle). According to the histological examination the specific inflammations were almost completely, if not completely, inactive. In the third case an active, subacute, syphilitic encephalitis was associated with a negative reaction in the serum. These results demonstrate the almost deadly accuracy of the Wassermann test when properly carried out, for in only 3 per cent. of the cases were there misdiagnoses, in the sense that syphilis was not diagnosed during life, although certainly or probably present. In the remaining 96·9 per cent.

of the cases the most searching inquiry failed to show that the diagnosis made during life was at fault.

Criticisms of the Value of the Test.

In spite of the fact that the accuracy of the Wassermann test has been established in an unusually large series of observations, a number of criticisms have been raised. In part, these appear as mere statements that it is inaccurate, or a few isolated observations have led certain writers to condemn the test altogether. In a few instances the indictment is much more formidable, inasmuch as serious discrepancies are alleged to have occurred where one and the same serum has been tested by different serologists. Thus Wolbarst (11) quotes the case of a young man who had no symptoms of syphilis with the exception of a suspicious throat lesion some years previously. His blood was sent to two laboratories; A returned a negative result, B a 4+result. A second sample of blood taken three days later was divided into three portions, of which one was sent to A, and two were sent to B. The report of A was 'negative'; the report of B was 1+. Wolbarst quotes the following result of eleven other cases, in which one and the same serum was tested by two different serologists:

	Serologist	*Serologist*	*Clinical diagnosis*
1.	A = +	B = –	not syphilis
2.	A = +	B = –	,, ,,
3.	A = +	B = –	,, ,,
4.	A = +	C = –	,, ,,
5.	C = +	E = –	syphilis
6.	A = +	A = ?	not syphilis
7.	A = +	A = ?	syphilis
8.	A = –	A = ?	,,
9.	A = –	A = ?	not syphilis
10.	A = –	A = ?	,, ,,
11.	C = –	A = ?	,, ,,

From results like these Wolbarst concluded that it was a gross error to accept the findings of one serologist as conclusive, particularly if the result is positive and the diagnosis dependent on his work. He also quotes without details the results of 37 other cases studied for discrepancies:

Agreement between the serologists took place in 26=70 per cent.
Complete contradiction ditto 5=14 per cent.
Slight disagreement ditto 6=16 per cent.

In a later paper (22) he comments on the results of 85 examinations of sera, where three examples taken at one and the same time were submitted with a few hours' delay to three different serologists of experience and reputation. The results were:

Serologist	*% of positive results*	*% of negative results*
A	73	27
B	27	73
C	50	50

In the 33 cases in which absolute contradictions were reported

Serologist A obtained 24+ (73 %) and 9− (27 %)
,, B ,, 9+ (27 %) and 24− (73 %)
,, C ,, 16+ (50 %) and 16− (50 %)

,, A ,, 9+ in sera declared − by B and C
,, B ,, 4+ ,, ,, − ,, A ,, C
,, C ,, 4+ ,, ,, − ,, A ,, B
,, B ,, 12− ,, ,, + ,, A ,, C
,, C ,, 4− ,, ,, + ,, A ,, B
,, A did not obtain a single − in serum declared + by his colleagues.

It is stated that serologist A used the Wassermann technique except that the quantities were reduced to one-tenth of the original, and the fixation was carried out in the ice box for four hours. B and C used the Wassermann as described by Citron.

In 1915 Phelps (18) published a preliminary report of Wassermann tests simultaneously performed in four laboratories, although no data are given respecting either the technique employed or the degree of discrepancy:

Four laboratories tested each of 113 sera: the results agreed in 68 instances = 60·2 per cent., and disagreed in 45 = 39·8 per cent.
Three laboratories tested each of 135 sera; the results agreed in 70 instances = 51·9 per cent., and disagreed in 65 = 48·1 per cent.
Two laboratories tested each of 110 sera; the results agreed in 72 instances = 65 per cent., and disagreed in 38 = 34 per cent.

Uhle and Mackinney (21) (1915) carried out in detail an important investigation along the same lines. Sera were collected under identical conditions from about 300 patients, and they were at first examined by four serologists, and later by three more. These serologists were all connected with teaching institutions and hospitals. They are distinguished in the following by the letters A, B, C, D, E, F, and G. Of these, all with the exception of E and F submitted 1 report. E submitted 2 reports with 2 different antigens, these were labelled E_1 and E_2; F, using three different antigens, submitted three reports which were labelled F_1, F_2, and F_3; while G, using three different antigens, submitted a majority report.

Blood was collected from 25 normal people who denied syphilis, from 70 private or hospital patients suffering from diseases other than syphilis, and from 197 patients suffering from different forms of syphilis. All these cases were under the personal observation of the authors, and the Wassermann reaction had been tested before the special inquiry was begun. In the syphilitic cases a clinical expectancy of 'positive', 'negative', or 'doubtful' was determined before the specimen was submitted, and of the findings the serologist was not informed. This clinical expectancy was based on a personal knowledge of the case, the type and activity of treatment, and the results of previous Wassermann tests. Where two or more specimens were sent from the same patient at the same time different names were used. The test was therefore carried out under entirely objective conditions.

In the group of 25 normal persons 27 series of tests were carried out, with no less than 5 reports in each series. All the serologists agreed in a negative report in 21 series and disagreed in 6. In each instance of disagreement, a positive report was not submitted by more than one laboratory. In 2 cases in which the tests were repeated, one serologist reported in one case first a + then a —, while in a second case, another serologist reported first a — and then a +.

On 70 persons suffering from conditions other than syphilis, 74 tests were made. In 4 of these the reports varied considerably, two or more positive results being obtained by different serologists in each case. The serum of one of these was examined four times, with the following interesting result:

1st examination	4 positive reports	0 negative report
12 days later	3 ,, ,,	2 ,, ,,
Next day	5 ,, ,,	1 ,, ,,
6 weeks from 1st examination	2 ,, ,,	4 ,, ,,

On account of the numerous positive reactions this patient was repeatedly questioned about a possible syphilitic infection, but denied it. The luetin test was negative. Examining in detail the Wassermann results carried out on this patient it was found that

Laboratory E gave consistently + reports
,, A ,, 1 + and 3 — ,,
,, B ,, 2 + and 1 — ,,
,, C ,, 2 + and 1 — ,,
,, D ,, 1 +, then —, then +, and finally —

The blood of a second patient examined in a similar manner showed

at first examination 4 negative and 1 positive result;
at second ,, 6 ,, ,, 2 ,, results.

In a third patient there were 4 positives and 2 negatives; while in a fourth patient there were 6 positives, 2 negatives, 1 doubtful, and 1 anti-complementary report. This patient was referred to a neurologist with the diagnosis of cerebral tumour. The cerebrospinal fluid yielded 9 negative and 1 positive reaction in the hands of different serologists.

Of the remaining 66 patients whose sera were examined only once, all serologists agreed in a negative report 56 times. In 10 cases one serologist disagreed with the others in submitting a positive report.

In the group of 197 cases of syphilis in all stages, 40 series of tests were made on 36 patients, the subjects of the primary, secondary, or tertiary stages of the disease. All the serologists agreed in a positive reaction in 25, and disagreed in 15 cases, With one exception, there was only 1 negative report in each of the tests which disagreed. This was a patient with a nodular syphilide of the leg, who responded to anti-syphilitic treatment. Of the remaining 14 tests which differed, a repetition was carried out in 4. In each case the second test gave a + report by the serologist who at the first had reported a negative reaction.

Syphilis of the eye and nervous system gave very discordant results, for in a series of 41 tests there were 28 disagreements.

108 examinations were carried out on 88 persons, who were known to have had syphilis, but at the time had no manifestations. Many of them had been treated. Repeated examinations were carried out on 16 of these, 13 having 2, 2 having 3, and 1 having 4 examinations. In this series Uhle and Mackinney found the results so inconsistent, both from the same and from different laboratories, that they scarcely admitted of analysis.

With regard to the technique employed, it is stated that four of the serologists used a specific antigen, one used 2 separate cholesterin antigens, while one used 2 cholesterin antigens and 1 specific antigen, i. e. 3 in all.

Uhle and Mackinney set out their figures in the following tables, which, however, are not very lucid:

TABLE I.—NORMAL AND NON-SYPHILITIC CASES.

No. of tests	*Serologist*	*Negative Results*	*Doubtful*	*Anti-complementary*	*Positive*				*Negative per cent.*	*Positive per cent.*
					+	+ +	+ + +	+ + + +		
107	A	93	6	0	5	3	0	0	86.8	7·4
97	B	91	0	2	1	2	1	0	91·7	4·1
64	C	59	0	1	0	3	1	0	92·1	6·2
96	D	71	1	9	10	0	3	2	73·9	15·6
97	E_1	88	1	0	0	3	2	3	90·7	8·2
87	E_2	79	1	0	0	3	2	2	90.8	8·0
33	F_1	32	0	0	1	0	0	0	96·9	3·1
11	F_2	8	1	0	1	1	0	0	72·1	18·1
32	F_3	30	1	0	1	0	0	0	93·7	3·1
38	G	36	1	0	1	0	0	0	94·7	2·5

TABLE II.—PERCENTAGE RESULTS OF 56 CASES, EXAMINED BY ALL LABORATORIES COMPARED WITH CLINICAL EXPECTANCY.

Positive expectancy		*Negative expectancy*		*Doubtful expectancy*	
Serologist	*Positive per cent.*	*Serologist*	*Positive per cent.*	*Serologist*	*Positive per cent.*
A	44·8	A	0	A	11·1
B	27·5	B	0	B	0
C	31·0	C	0	C	11·1
D	75·8	D	33·3	D	66.6
E_1	55·1	E_1	5·5	E_1	44·4
E_2	55·1	E_2	5·5	E_2	44·4
F_1	37·9	F_1	11·1	F_1	11·1
F_2	68.9	F_2	27·7	F_2	77·7
F_3	44·8	F_3	5·5	F_3	22·2
G	27·5	G	0	G	11·1

Uhle and Mackinney concluded from this that 'all the laboratories agreed in 21 per cent.; they disagreed materially in 19 per cent., and varied in from 1 to 4 of the 10 results in 60 per cent.

Of the latter, 20 per cent. varied in 1 test, 20 per cent. in 2 tests, 12 per cent. in 3 tests, and 8 per cent. in 4 tests. In other words, if a specimen of blood from the same individual be submitted to 10 tests by different serologists there is 1 chance in 5 that the tests will agree.'

TABLE III.—COMPARISON OF 168 TESTS REPORTED BY LABORATORIES A, B, C, D, E$_1$, AND E$_2$.

No. of tests	*Serologist*	*Negative*	*Doubtful*	*Anti-complementary*	*Positive*				*Positive per cent.*
					+	++	+++	++++	
168	A	98	13	0	8	7	2	40	33
168	B	113	0	7	9	5	5	29	28
168	C	124	2	1	3	20	4	14	24
168	D	79	0	2	23	13	15	36	51
168	E$_1$	96	3	0	7	14	7	41	41
168	E$_2$	94	3	0	0	16	10	45	42

An analysis shows that all laboratories agree in their findings in 47 per cent. They vary in one result in 20 per cent., in 2 results in 12 per cent., and in more than 2 results in 21 per cent.

Uhle and Mackinney conclude their investigation by remarking that the results of the Wassermann test are disappointing. 'When', they say, 'we find that various representative serologists report positive findings in from 2 to 18 per cent. of normal individuals, and that in active syphilis in which the clinical diagnosis is certain some serologists report only 50 per cent. of positive results, there is every reason to discredit the diagnostic value of the test. In suspected latent syphilis, and in syphilis under active treatment, the most extreme variations occur, and in these conditions, in which the clinician needs its help the most, it is the least accurate.'

Very different conclusions were reached in 1916 by Simons, Jones and Goddard (34) as the result of a combined investigation carried out on 1000 specimens, viz. 981 sera and 19 cerebro-spinal fluids. These specimens were examined simultaneously by Simons and Jones in the Bacteriological Laboratory of the Vanderbilt University (Nashville, Tenn.) and by Goddard in the Laboratories of the Board of Health of the State of Tennessee. The latter used as antigen an acetone insoluble fraction of the lipoids of beef heart (Noguchi's antigen); Simons and Jones used a similar antigen for the first 535 tests and Coca and L'Esperance's antigen for the remaining 465 tests. The general agreement in the two series of tests was very striking.

Laboratory	*No. of tests*	*Positive reactions*	*% of positive*
Board of Health	1000	218	21·8 %
Vanderbilt University	1000	223	22·3 %

The specimens were also divided into three series as follows.

Table I.—Results obtained in 1000 Wassermann Tests when each Laboratory used its own Reagents.

Series	Reports agreed in	Board of Health report showed increased positivity in	Vanderbilt Univ. report showed increased positivity in
Series I	(343 cases) 92·2 %	13 cases . . 3·4 %	16 cases . . 4·3 %
„ II	(267 „) 94·0 %	11 „ . . 3·8 %	6 „ . . 2·1 %
„ III	(325 „) 94·5 %	6 „ . . 1·7 %	13 „ . . 3·8 %
935	93·5 %	30	35

Table II.—Results obtained in 628 Wassermann Tests when both Laboratories used the Antigen supplied by the Board of Health.

Series	Reports agreed in	Board of Health report showed increased positivity in	Vanderbilt Univ. report showed increased positivity in
Series II	(266 cases) 93·6 %	11 cases . . 3·8 %	7 cases . . 2·4 %
„ III	(327 „) 95 %	3 „ . . 0·8 %	14 „ . . 4·0 %
593	94·3	14	21

Table III.—Results obtained in 628 Wassermann Tests when both Laboratories used the Antigen supplied by the Vanderbilt University.

Series	Reports agreed in	Board of Health report showed increased positivity in	Vanderbilt Univ. report showed increased positivity in
Series II	(266 cases) 93·6 %	13 cases . . 4·5 %	5 cases . . 1·7 %
„ III	(330 „) 95·9 %	2 „ . . 0·5 %	12 „ . . 3·4 %
596	94·7	15	17

From these results Simon, Jones, and Goddard concluded that when the reactions are carried out with proper technique by two laboratories a very high percentage of agreements should be reached. In their series it was 93·5 % in 1000 tests. The divergences, which amounted to 6·5 %, are due to the difficulty in the standardization of the sheep blood, complement and amboceptor, inasmuch as higher results were obtained when both laboratories used the same reagents (compare results in Table I of Series I and Series III). More of this error was eliminated when in addition to this the same antigen was used by both laboratories (compare the results of Series III in Tables I, II, and III).

The paper of Uhle and Mackinney created a great deal of interest in America, and was followed by a number of communications, mostly of minor importance, in which the discrepancies in Wassermann results were emphasized. Both serologists and clinicians took part in the discussion, as the result of which Dr. Haven Emerson, deputy-commissioner of health of New York city, summoned a committee to consider the whole question of the reliability of the Wassermann reaction, and to attempt to standardize the technique. The committee, composed of professional serologists in the leading medical institutions in New York, held many meetings, but its work was not completed. Apparently the chief difficulty was that, although no two members agreed precisely in the technique of any single step in the reaction, each considered that he was working along classic principles with a technique which he regarded as efficient. With the exception of Coca, all the other members of the committee considered that in the vast majority of cases the Wassermann reaction is reliable, and, with a few well-known and easily-excluded exceptions, is diagnostic of syphilis; that most of the few instances in which contradictory reports were received from different serologists were actually cases of syphilis showing weak reactions detectable by certain forms of technique, but not by others, and that when all precautions are taken false positive reactions are avoidable. In the last two or three years a number of publications have appeared in the United States commenting on the complexity of the test, and emphasizing the necessity for standardization, but up to the present time no one method has been considered to be the standard one.

In Great Britain the reports of discrepancies in the Wassermann tests led to a similar state of affairs, and the Medical Research Committee appointed a Standards Sub-committee, which after much deliberation issued a report (Special Report Series, No. 14, 1918) in which three methods were recognized as conforming more or less closely to the condition of a 'standard' in the present state of knowledge. Whether the criticism of the Wassermann test as performed in England is general or not is not known, but so far very little that is of value on the subject has been published.

The study of German medical literature during the war has revealed that similar doubts as to the reliability of the Wassermann reaction have been the subject of discussion. Even in 1910 Freudenberg (2) published a warning on the unreliability of the Wassermann test, and quoted two cases in support of his contention. In one the serum of a man who had had syphilis was examined on three different dates by one or more of four different serologists as follows:

Date	*A*	*B*	*C*	*D*
Jan. 19, 1909	–			
April 2, 1909		+		
Nov. 11, 1909		+	+	–

In the other, who had a sore on the penis, in which, however, no spirochaetes were found, the results were equally discordant:

Date	*B*	*C*	*D*	*E*
Oct 26, 1909	+			
Oct. 29, 1909		–		
Nov. 4, 1909	+	+	–	–

In the same year Saalfeld, having had a like experience, proposed in the Berlin Medical Society that some sort of standardization should be carried out under State control in order to lessen, if possible, the divergent results. His proposal was not accepted.

In 1916 (33) he returned to the subject and cited three cases in which discordant results were returned. In one case one serologist returned a serum as '+ +', another as '–', and still another said the result was + in active but – in inactivated serum. In the second case one laboratory returned the result as + + + +, two others as –, while a fourth gave + in active and – in inactive serum. In the third case one laboratory gave a 4 + result, two others a –.

Freudenberg (31), 1916, who had also been continuing his observations, recorded the results in 144 sera examined by two or more serologists simultaneously. Altogether twelve different persons carried out the tests, which were entirely objective. The results were as follows:

In 4 cases where 4 serologists tested each serum differences were obtained 3 times = 75 per cent.
In 44 cases where 3 serologists tested each serum differences were obtained 26 times = 59·1 per cent.
In 96 cases where 2 serologists tested each serum differences were obtained 17 times = 17·7 per cent.

These divergences were not slight, as, e. g., between + and ±, or – and ±, but were mostly complete contradictions, as, e. g., + versus –.

In six years Freudenberg emphasized the fact that there had been no real improvement in the results, because, analysed from a chronological standpoint, the percentage of divergences remained practically constant. Thus, dividing the 144 sera into 4 quarters as regards the dates of examination, he found—

1st quarter	36 tests with	12 divergences	= 33·3 per cent.
2nd ,,	36 ,, ,,	12 ,,	= 33·3 per cent.
3rd ,,	36 ,, ,,	10 ,,	= 27·8 per cent.
4th ,,	36 ,, ,,	12 ,,	= 33·3 per cent.

Heller (32), 1916, who was in charge of the venereal department of a military hospital, had sera to the number of 87 tested in two well-known laboratories, viz. that of Prof. L. Pick and that of Ledermann. The following were the results obtained:

1. Cases in which identical results were returned = 36
2. Cases in which there was a difference in the interpretation of the result (e. g. weak + or –) = 5
3. Cases in which there were differences in the degree of reaction = 30
4. Cases in which directly contrary results were returned = 16

Of these 16 Ledermann had 10 negative, and Pick 6, while the Control Institute gave positive results. Heller considered that the Wassermann results break down exactly in the cases where help is most required, and he quotes a few instances in which the results were quite at variance with the clinical experiences and history. He believed that the fault lay not so much with the serologist as with inherent defects in the method employed to test the serum.

Wassermann himself here entered the lists and strongly and adversely criticized the publications of Heller, Freudenberg, and Saalfeld, and was particularly indignant at their suggestion that the Wassermann reaction is untrustworthy because different results were obtained when one and the same serum was tested by different serologists. These divergent results had been used both in the medical and lay press to discredit the test. In order to clear the matter up Wassermann (56) suggested a combined test by two different workers in two reputable institutes, viz. Dr. Mohrmann in the Kaiser Wilhelm Institut für Experimentelle Therapie and Dr. Lange in the Kaiser Wilhelm Akademie für das militärärztliche Bildungswesen. Wassermann stipulated that all sera giving an absolute or almost absolute inhibition of haemolysis (+ + + +; + + +) were to be returned as 'positive', whereas all sera which showed complete haemolysis were to be returned as 'negative'. All sera between these limits of haemolysis (such degrees as + +; ±) were to be returned as 'doubtful'. The sera were collected by Heller, who transmitted them to Prof. Bickel, who then sent them numbered to the two testers. Of 50 sera tested in this way 48 showed complete harmony in the results. Of the remaining two, one was returned as 'negative' by one observer and 'doubtful' by the other, the remaining serum as 'positive' by one observer and 'doubtful' by the other. In these results Wassermann saw a complete confirmation of his view that in the hands of trustworthy workers the Wassermann test is extraordinarily accurate. In his reply Freudenberg (51) draws attention to the frequence of 'doubtful' reactions in the diagnosis of syphilis, and the difficulty in determining the significance of reactions returned as ±. In Wassermann's series of 50 sera tested by two independent observers, the one found 'doubtful' reactions six times, the other eight times = 14 per cent., which was seven times as large as the 'doubtful' sera tested by G. Meier in another series. Freudenberg also repudiated Wassermann's suggestion that divergence of result is largely due to the personal equation of different observers or defective technique, and he now published the names of twelve serologists whose results had been divergent. Some of these were widely known for their special work in connexion with the Wassermann test, and in some cases had been actual pupils of Wassermann himself. Freudenberg then analysed the results where one tester had been opposed by a number of others in examining the same sera, and estimated the number of times that harmony (=) and divergence (<) was noted. Thus a well-known serologist, Dr. Georg Meier (B), examined a number of sera (72), which were examined at the same time by nine others (A, C, D, E, F, G, H, I, L) with the following results:

Observers	*Number of tests*	*Results*		*Divergences* (<)					
		=	<	+ : −	+ : ±	± : −	− : +	± : +	− : ±
B : A	38	24	14	1			12	1	
B : C	5	3	2	1			1		
B : D	6	3	3				2		1
B : E	9	8	1				1		
B : F	1	—	1				1		
B : G	7	7	—						
B : H	2	1	1	1					
B : I	3	2	1	1					
B : L	1	1	—						
9 combinations	72	49	23	4			17	1	1

From the table it is seen that 'B' (Dr. Georg Meier) when opposed to 9 other testers agreed completely in his results with only 2 of them, and in one case only 1 serum was tested (B : L). In other partnerships it is seen that he differed 14 times in 38 tests.

In another series Dr. Hermann Mayer (L) was pitted against six other serologists in a test of 63 sera with the following results:

Observers.	*Number of tests*	*Results*		*Divergences* (<)					
		=	<	+ : −	+ : ±	± : −	− : +	± : +	− : ±
L : A	33	22	11	3			7	1	
L : B	1	1	—						
L : D	1	—	1				1		
L : G	8	7	1	1					
L : I	13	12	1	1					
L : M	7	5	2	1			1		
6 combinations	63	47	16	6			9	1	

Here it will be seen that complete agreement was attained with one opponent only, and it is unfortunate that only 1 serum was the subject of the test. In the case of another opponent 11 divergences were recorded in the case of 33 sera tested. Freudenberg writes at considerable length on the value of these comparative tests, and repudiates the idea that the disparity is due to the tester alone. He refers it much more to variations in the test material, especially the antigen, and he cites a result obtained by G. Meier (of the date 8·ix·1910!) who with 2 alcoholic extracts found a − result, with a watery extract a ±, and with still another extract tested on the following day a complete positive result, viz. + + + +. The case was some disorder of micturition on a doubtful luetic spinal basis.

He also considers that part of the divergence is attributable to certain sera rather than others; a disparity once observed was very apt to recur again and again in the reports of different testers. He publishes a table of one such serum as follows, the case being stated to be undoubted syphilis:

Date	*A* *Dr. Mühsam*	*B* *Dr. G. Meier*	*D* *Dr. Klopstock*	*G* *Dr. Lindenheim*	*K* *Dr. Lilienthal*	*L* *Dr. H. Mayer*	*Uniformity* (=) *Divergence* (<) *in results*
Dec. 19, 1908	weak +						
May 11, 1910	+						
June 25, 1912	weak +	−					<
Jan. 14, 1913	strongly +	−					<
Jan. 30, 1913	,, +			−		weak +	<
July 16, 1913	+	−		−		−	<
July 19, 1913	+	−	weak +			−	<
July 6, 1916	−		−		weak ±		= (<)

Hermann Mayer (58) criticizes the reasoning of Freudenberg, and points out the fallacy of comparing 38 sera on the one hand with

1 serum on the other. He also points out that Freudenberg has eliminated the almost complete harmony of certain of the testers while he emphasizes the discordant results of others. The want of uniformity, especially in the series in which tester A collaborated, is attributed to the use of heart extract instead of liver extracts, and he considers that as a diagnostic agent the Wassermann reaction gives wonderfully accurate and almost constant results. This is, however, denied by Freudenberg (59).

Heller (52) also replied to Wassermann's criticism, and published a complete list of the fifty cases referred to by Wassermann. In addition to the two tests made in Lange's and Wassermann's laboratories he had taken the precaution to have a third portion of each serum tested in another laboratory X, the tests being carried out by a well-known expert. Of the 50 sera 48 were tested by all three examiners. The general results were as follows:

Complete agreement	22	cases	=	46 per cent.
Differences	26	,,	=	54 per cent.
Complete contrary results	9	,,	=	19 per cent.
Considerable differences	3	,,	=	6 per cent.
Slight differences	14	,,	=	29 per cent.

In the table it will be seen that the comparative serological results are given, the clinical diagnosis by Heller or others, and the estimate which of the three serological tests agreed best with the clinical facts.

No.	*Clinical diagnosis*	*W. R. before treatment was begun*		*Results of Lange (L)*	*Results of Wassermann (W)*	*Results of Institut 'X'*	*Serological divergences*	*Serological result in closest agreement with clinical diagnosis*
1	Ulcus molle			neg.	neg.	neg.		
2	Typical sclerosis in course of development	neg.	pos.	neg.	neg.	neg.		
3	Ulcus molle			neg.	neg.	neg.		
4	Tertiary syphilis—extensive skin lesions			doubtful	doubtful	pos.	!	X
5	Hysteria—clinically no nerve syphilis		pos.	pos.	pos.	doubtful	!	
6	Sclerosis—syphilis			pos.	pos.	pos.		
7	Tertiary syphilis			pos.	pos.	pos.		
8	Ulcera mollia			neg.	neg.	neg.		
9	Developing sclerosis			pos.	pos.	doubtful prob. +		
10	Syphilis, sclerosis			neg.	neg.	neg.		
11	Syphilis—end of cure			neg.	neg.	pos.	!!!	
12	Syphilis primary and secondary			pos.	pos.	pos.		
13	” ” ”			pos.	pos.	pos.		
14	Clinical sclerosis (no spirochaetes)			doubtful	doubtful	doubtful		
15	Syphilis			pos.	pos.	pos.		
16	Sclerosis, syphilis			neg.	neg.	doubtful prob. +	!!	X
17	Compare no. 5			pos.	pos.	pos.		
18	Syphilis formerly		pos.	neg.	neg.	doubtful	!	
19	Syphilis, sclerosis			neg.	neg.	pos.	!!!	X

20	,, ,,			neg.	neg.	pos.	! ! !	X
21	,, ,,			neg.	neg.	pos.	! ! !	X
22	,, ,,			neg.	neg.	doubtful	! !	X
23	Syphilis			pos.	pos.	pos.		
24	,,	I pos. III doubtful	II neg.	neg.	neg.	neg.		
25	Not syphilis			neg.	neg.	neg.		
26	Syphilis (cure finished)			neg.	neg.	anti-complementary	!	
27	,, ,, ,,			neg.	neg.	doubtful		
28	,, ,, ,,			doubtful	doubtful	pos.	!	
29	Not syphilis	doubtful		neg.	neg.	pos.	! ! !	L. W.
30	Sclerosis			doubtful	doubtful	*not done*		
31	Lues			neg.	neg.	doubtful	!	
32	Chancre—not syphilis			neg.	neg.	neg.		
33	,, ,,			neg.	neg.	pos.	! ! !	L. W.
34	,, ,,			neg.	neg.	doubtful	!	L. W.
35	Syphilis			pos.	pos.	pos.		
36	Clinically not syphilis	pos.	pos.	neg.	doubtful	doubtful	!	
37	Chancre			neg.	neg.	neg.		
38	Clinically not syphilis	pos.	pos.	pos.	pos.	doubtful	!	
39	Clinically not syphilis (said to have had S.)		pos.	pos.	doubtful	neg.	! ! !	
40	Chancre			doubtful	doubtful	neg.	!	
41	Cerebral syphilis (?)			neg.	neg. ?	doubtful slight +	! !	
42	Chancre			neg.	neg.	neg.		
43	Sclerosis			neg.	neg.	doubtful slight +	! !	
44	Ul. phagæd.			neg.	neg.	neg.		
45	Gonorrhoea, epilepsy, malaria	neg.	neg.	pos.	pos.	neg.	! ! !	*
46	Syphilis formerly			pos.	pos.	doubtful prob. +	!	
47	Syphilis			pos.	pos.	neg.	! ! !	L. W.
48	,,			pos.	pos.	pos.		
49	Gonorrhoea			neg.	neg.	neg.		

* Probably an error, given in Wassermann's series as 'negative'.

REFERENCES.

[All these papers have been consulted by Dr. Bulloch with the exception of those marked * which were inaccessible.]

1. **Bassett-Smith**: The diagnosis of syphilis by the complemental deviation method. *Brit. M. J.*, Lond., 1910, II, 1434.
2. **Freudenberg**: Eine Mahnung zur Vorsicht bei der diagnostischen Verwertung der Wassermann'schen Syphilisreaktion. *Berl. klin. Wchnschr.*, 1910, **47**, 1231.
3. **Garin** et **Laurent**: 200 cas de réaction de Wassermann. *Presse méd.*, Par., 1910, **18**, 501.
4. **Harrison, L. W.**: Article in Power and Murphy's 'System of Syphilis'. London, 1910, VI, 173.
5. **Wassermann**: The diagnostic use of the complement fixation method. *Brit. M. J.*, Lond., 1910, II, 1427.
6. **Browning** and **Mackenzie**: Recent methods in the diagnosis and treatment of syphilis. London, Constable, 1911, pp. xxxvi + 303.
7. **Fildes** and **McIntosh**: The Wassermann reaction and its application to neurology. *Brain*, Lond., 1913, **36**, 193.
8. **Major, R. H.**: The Wassermann reaction in the Johns Hopkins Hospital. *Johns Hopkins Hosp. Bull.*, Balt., 1913, **24**, 175.
9. **Müller, Rudolf**: Die Serodiagnose der Syphilis und ihre Bedeutung für die Diagnose, Therapie und Prognose. Wien, 1913. 171 S.
10. **Pusey**: Unreliable Wassermann reactions. *J. Am. M. Ass.*, Chicago, 1913, 61, 1920.
11. **Wolbarst**: Contradictory findings in the Wassermann test. *New York Med. Journ.*, 1913, **97**, 378.
12. **Boas**: Die Wassermannsche Reaktion mit bes. Berücksichtigung ihrer klinischen Verwertbarkeit. 2nd edit., Berlin, 1914.
13. **Leredde** et **Rubinstein**: Sérodiagnostique de la syphilis; specificité de la réaction de Wassermann; serums paradoxaux. *Bull. Soc franç. de dermatol. et syph.*, Par., 1914–15, **25**, 379.
14. **Nicolas** et **Gaté**: La réaction de Wassermann positive, a-t-elle une valeur absolue? 39 p. 100 de réactions positives chez les non-syphilitiques. *Bull. Soc. franç. de dermatol. et syph.*; Par., 1914, **25**, 200.
15. **Southard**: Statistical notes on a series of 6000 Wassermann tests for syphilis performed in the Harvard Neuropath. testing laboratory, 1913. *Boston M. and S. J.*, 1914, **170**, 947.
16. **Stone, C. T.**: Sources of error in the Wassermann technique. *N. York M. J.*, 1914, **99**, 1242.
17. **Craig, C. F.**: The results and interpretations of the Wassermann test. *Am. J. M. Sc.*, Phila., 1915, **149**, 41.
18. **Phelps, O. D.**: A preliminary report of the result of the Wassermann tests as reported from different laboratories, &c. *Boston M. and S. J.*, 1915, **173**, 391.
19. **Schlesinger, M. F.**: Reasons for discrepancies in reports of the Wassermann reaction from a technician's side. *Med. Rec.*, N. Y., 1915, **87**, 61.
20. **Thomas, G. E.**: Result of Wassermann and luetin tests at the Naval Prison, Portsmouth N. H. *Med. Rec.*, N. Y., 1915, **87**, 523.
21. **Uhle** and **Mackinney**: Comparative results of the Wassermann test. *J. Am. M. Ass.*, Chicago, 1915, **65**, 863.
22. **Wolbarst**: A further clinical study of the contradictory findings in the Wassermann test. *Interstate M. J.*, St. Louis, 1915, **22**, 109; also in *Am. J. Urol.*, N. Y., 1915, **11**, 143.
23. **Allen, A. H.**: The diagnosis of syphilis by the Wassermann reaction. *U. S. Nav. M. Bull.*, Wash., 1916, **10**, 304.

24. Bassett Smith: The complement deviation (Wassermann's reaction) for syphilis and some comments on irregularities noticed in practical experience. *J. Roy. Nav. M. Serv.*, Lond., 1916, **2**, 282.

25. Bruhns: Ueber unbewusste Spätsyphilis nebst Mitteilungen über Ausfall der Wassermannschen Reaktion an 1800 angeblich nicht mit Syphilis inficierten Menschen. *Berl. klin. Wchnschr.*, 1916, **53**, 833.

26. Bryan, W. M.: Prevalence of syphilis as indicated by the routine use of the Wassermann reaction. *Pub. Health Rep.*, Wash., 1916, **31**, 3230.

27. Buhman, R.: Specificity of the Wassermann reaction. *Tr. Am. Gynec. Soc.*, 1916, **41**, 319.

28. Coca, A. F.: The clinical significance of the Wassermann test. *J. Immunol.*, Balt. and Cambridge [Eng.], 1916, **1**, 484.

29. Fildes, P.: The prevalence of syphilis among apparently healthy adult inhabitants of the East End of London. Roy. Commission on Venereal Diseases. Final Report, 1916, App. XII, 139.

30. Fonss, A. L.: The defects of Wassermann's reaction. *Canad. Pract. and Rev.*, Toronto, 1916, **41**, 155.

31. Freudenberg: Nochmals eine Mahnung zur Vorsicht bei der diagnostischen Verwertung der Wassermann Reaktion. *Berl. klin. Wchnschr.*, 1916, **53**, 1154.

32. Heller: Kritisches zur modernen Syphilislehre. *Berl. klin. Wchnschr.*, 1916, **53**, 978.

33. Saalfeld: Zur Ausführung der Wassermannschen Reaktion in der Praxis. *Deutsche med. Wchnschr.*, Berl. u. Leipz., 1916, **42**, 1351.

34. Simons, Jones and Goddard: The margin of error in the Wassermann test (a study of 1000 tests made independently by two laboratories). *Interstate M. J.*, St. Louis, 1916, **23**, 654.

35. Smith and MacNeal: A comparative study of different methods of performing the Wassermann test for syphilis. *Proc. Soc. Exp. Biol. and Med.*, N. Y., 1916–17, **14**, 7; also *J. Immunol.*, Balt. and Cambridge [Eng.], 1916, **2**, 75.

36. Uhle and Mackinney: A clinical study of the comparative results of the Wassermann reaction. *Boston M. and S. J.*, 1916, **174**, 55.

*37. Uhle and Mackinney: A further study of the comparative results of the Wassermann test. *Med. Times*, N. Y., 1916, **44**, 301.

38. Ball, C. R.: A consideration of the serobiologic reactions after five years of observation. *J. Am. M. Ass.*, Chicago, 1917, **68**, 262.

39. Bronfenbrenner and Schlesinger: Conclusions drawn from a comparative study of different methods of performing the Wassermann reaction. *N. York M. J.*, 1917, **106**, 489.

40. Clark and Nelson: The value of the Wassermann reaction in the diagnosis and treatment of syphilis. *Canad. Pract. and Rev.*, Toronto, 1917, **43**, 345.

41. Craig: The practical application of the Wassermann test in the diagnosis and control of treatment of syphilis. *Am. J. Syph.*, St. Louis, 1917, **1**, 192.

42. Darling, Georgina R.: The Wassermann test as a means of estimating the prevalence of syphilis in a community. *Dublin J. M. Sc.*, 1917, **144**, 147.

43. East, G. R.: The Wassermann reaction. *Brit. M. J.*, Lond., 1917, II, 777.

44. Gehrmann: The diagnosis of syphilis from specimens sent to the laboratory. *Am. J. Pub. Health*, N. Y., 1917, **7**, 964.

45. Gordon, A. Knyvett: The clinical significance of laboratory tests for syphilis. *West London M. J.*, Lond., 1917, **22**, 62.

46. Kaplan: The four plus Wassermann. *N. York M. J.*, 1917, **105**, 728.

47. Knapp, E. V.: Wassermann reaction in 400 cases investigated by group study methods. *Am. J. Syph.*, St. Louis, 1917, **1**, 772.

48. Leredde et Rubinstein: Quelle valeur le praticien doit-il accorder, à la séro-réaction de la syphilis. *Rev. gén. de clin. et de thérap.*, Par., 1917, **31**, 481, 500.

49. Ottenberg, R.: On the reliability of the Wassermann reaction; a study of the sources of error and an attempt to standardize the technic. *Arch. Int. Med.*, Chicago, 1917, **19**, 456.

50. Schmidt, L. E.: Clinical value of the blood Wassermann test. *Chicago M. Rec.*, 1917. **39**, 185.

51. Freudenberg, A.: Zur Zuverlässigkeit der Wassermannschen Reaktion bei Syphilis. *Berl. klin. Wchnschr.*, 1917, **54**, 303.

52. Heller, Julius: Zur Frage der Zuverlässigkeit der Wassermannschen Reaktion. *Berl. klin. Wchnschr.*, 1917, **54**, 306.

*53. Scheel, V: The importance of the Wassermann reaction for the internal clinic. *Ugesk. f. Laeger*, Kjóbenhavn, 1917, **79**, 43.

54. Slack, Castleman, and Bailey: A year's work with the Wassermann test in the Boston Health Department Laboratory with special reference to doubtful reactions. *Boston M. and S. J.*, 1917, **177**, 180.

*55. Sonntag, Erich: Die Wassermansche Reaktion in ihrer Serologischen Technik und Klinischen Bedeutung. Berlin, 1917, 191 S.

56. Wassermann: Zur Frage der Zuverlässigkeit der Wassermannschen Reaktion. *Berl. klin. Wchnschr.*, 1917, **54**, 105.

57. Wohl, M. G.: A clinical consideration of the Wassermann reaction. *Medicine and Surgery*, St. Louis, 1917, **1**, 303.

58. Mayer, Hermann: Zur Frage der Divergenz der Wassermann Resultate. *Berl. klin. Wchnschr.*, 1918, **55**, 86.

59. Freudenberg: Zur Frage der Divergenz der Wassermann Resultate. *Berl. klin. Wchenschr.*, 1918, **55**, 620.

II. REPORT ON THE WASSERMANN REACTIONS

Obtained in 104 *Cases by*

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Compiled by

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§ 1. *Object.*—The object of this inquiry is to compare the results of the Wassermann reactions performed by three well-known observers with a view to determining the relative value of their methods from the clinical standpoint.

§ 2. *Material.*—Between January 19 and April 10, 1918, 104 cases were used for this purpose. They were—

(*a*) 71 cases clinically syphilitic, in all stages, both treated and untreated, with the exception of young infants suffering from hereditary syphilis from whom it was deemed unwise to take so much blood as would be required for three separate examinations.

(*b*) 3 cases suspected to be syphilitic 'for diagnosis'.

(*c*) 30 cases clinically non-syphilitic, including—

Ulcus molle.
Lupus vulgaris.
Lupus erythematosus.
Tuberculous ulcer.
Leprosy.
Scleroderma.
Scabies.
Psoriasis.
Seborrhoides.
Erythema.
Eczema marginatum (Tinea cruris).
Furunculosis.
Carbuncle.
Diabetes.
Graves' disease.
Follicular tonsillitis.
Acute rheumatism.
Ulcerative endocarditis.
Osteomyelitis.

The responsibility for the diagnosis (except in ten medical and surgical cases) is mine.

The blood was drawn in each case from a vein into tubes of the type provided by the Local Government Board. The tubes were corked and enclosed in the wooden boxes supplied and sent direct to the three laboratories, those to the Middlesex Hospital and Rochester Row being forwarded through the post, and those to the laboratory of the London Hospital being sent by hand. Each specimen was numbered, but *no clinical details were sent.* In some instances the specimens were broken or failed to arrive at the laboratories, and in other cases some doubt as to numbering occurred. Where possible second specimens were sent. This was not always practicable owing to the non-return of the patients to the clinic. In six specimens in all, therefore, there are no reports.

§ 3. *A possible source of error.*—It is important to note that fresh sheep's blood is necessary for the examination, and that immediately prior to the rationing of meat in the Metropolitan area there were weeks in which no sheep were killed, and that there has been some difficulty in obtaining fresh blood throughout the period during which the examinations were made. It is well known that formalinized blood introduces a possibility of error, and it would be advisable to inquire whether such blood was used in the laboratories while the investigations were proceeding.

[On inquiry the Committee find that formalinized corpuscles were used during several weeks by Dr. McIntosh.]

Tables 1 to 11 record the results of the Wassermann reactions with the clinical factors briefly stated. Table 12 gives an analysis of the results in the syphilitic cases. Table 13 gives a summary of these results. Table 14 gives a detailed comparison of the results returned by the three observers in three groups.

The reports of the three observers vary in their descriptions of the types of reaction.

(1.) Dr. Browning classifies his results in five degrees:

+
+ Weak.
Very suspicious.
Suspicious.
—

He was good enough to explain the significance of these descriptions thus:—

Positive, excluding certain uncommon diseases, means syphilis. It is a result to which one would swear in a court of law.

Weak Positive:

(*a*) Is a 'moral' certainty, but one would not swear to it as positive in an unknown case.

(*b*) In a case of known syphilis which had previously reacted positive and which had then been treated, this result would, of course, rate as positive and would indicate the need for further treatment.

Suspicious or *Doubtful*:

(*a*) Means a reaction which in an unknown case would indicate the need for further investigation, e. g. if got in one child of a family it would prompt the examination of the other children.

(*b*) In a known treated case it would, of course, bear the same significance as 'weak positive'.

Negative, of course, leaves the issue entirely to the judgement of the clinician.

(2.) Colonel Harrison uses a series of symbols for which he has kindly forwarded the following interpretation. He recognizes six degrees of reaction:—

Positive reactions are of three grades:

+ + the strongest.
+ ± the next.
+ ordinary positive.

Any weaker reaction would not be considered sufficient for a diagnosis.

Doubtful reactions are of two grades:

$\pm$ $\overset{+}{\scriptscriptstyle - -}$

the latter being practically negative.

If the case is a treated one these reactions are considered indications for further treatment.

If the case has not yet been diagnosed the usual procedure after receiving a $\pm$ or $\overset{+}{\scriptscriptstyle - -}$ report is to give a provocative injection of '606' or '914' and test further samples, but the reaction must be returned + or stronger before a diagnosis is founded on it.

Negative reactions are indicated by the sign —.

(3.) Dr. McIntosh returns his results in four categories. He writes in reply to an inquiry:

> The results given are purely from the diagnostic aspect, as I understood the tests to be done were to test the specificity of the reaction, in fact qualitative rather than quantitative. Four degrees of reaction are recorded:
>
> (*a*) *Positive* (includes trace of haemolysis).
>
> (*b*) *Positive* (*incomplete*), weak positive.
>
> (*c*) *Negative* (*trace*) which is a negative result from the diagnostic view, but of value in a known syphilitic and especially in treated cases.
>
> (*d*) *Negative.* —.

TABLE I. SYPHILIS. PRIMARY. UNTREATED. 15 CASES.

Research No.	*Sex*	*Age*	*Site*	*Supposed duration*	*Dr. Browning*	*Col. Harrison*	*Dr. McIntosh*
7	M	53	penis	18 days	+	±	test unsatisfactory
10	M	30	penis	1 week	suspicious	—	negative (trace)
16	F	21	lower lip	2 weeks	very suspicious	—	—
20	M	42	penis phagedenic	14 days	+	+ +	+
29	M	27	penis	3 weeks	—	—	—
36	M	20	penis	3 weeks	+	+ +	+
42	F	22	labium	1 month	+	+ +	+
44	M	38	penis	3 weeks	+	+ +	+ (incomplete)
49	F	22	vulva	14 days	+	+ +	+
60	M	21	penis	10 days	+	+ +	+
65	F	22	vulva	5 weeks	+	+ +	+
66	M	22	penis	1 week	—	+ +	+
72	M	23	penis	1 month	+	+ +	+
73	M	20	penis	3 weeks	+	+ +	+
78	M	23	penis	1 month	+	+ +	+

TABLE II. SYPHILIS. PRIMARY. TREATED. 4 CASES.

Research No.	*Sex*	*Age*	*Site*	*Date*	*W. R. before treatment*	*Treatment*	*Dr. Browning*	*Col. Harrison*	*Dr. McIntosh*
33	M	31	penis spirochaetes	March 30, 1916	+	Galyl 0·3, 0·4, 0·4 Hg. 8 intramuscular	—	—	—
41	F	?	labium	1916	+	Galyl 0·3, 0·3, 0·4 Hg. 8 intramuscular, last July, 1917	—	—	—
59	M	26	penis	March 4, 1917	+	N.A.B. 0·6, 0·9, 0·9 Hg. 8 intramuscular last May, 1917	—	—	—
87	F	20	labium	July, 1917	+	N.A.B. 0·6, 0·6, 0·9 Hg. 8 intramuscular last Sept. 1917	—	—	—

N.A.B. = Novarsenobillon.

Table III. Syphilis generalized (Secondary) Untreated. 20 Cases.

Research No.	*Sex*	*Age*	*Site and date primary*	*Skin*	*Throat*	*Glands*	*Other points*	*Dr. Browning*	*Col. Harrison*	*Dr. McIntosh*
1	M	26	penis 9 weeks	polymorphic rash	ulcers	+	primary still present	+	+ +	+
3	F	22	labium ? duration	papular	nil	+	primary still present	+	+ +	+
6	F	37	no history	condylomata	ulcers	+	alopecia syphilitica	+	+ +	+
9	M	29	penis 2 years	papulo squamous	mucous patches	+		+	+ +	+
11	M	29	penis 9 months	nil	mucous patches, &c.	+		+	+ +	+
15	M	21	foreskin 6 weeks	profuse papulo squamous	mucous patches	+	headache + + insomnia	+	+ +	+
19	M	30	penis 6 months	profuse rupial in part	mucous patches	+		–	+ +	+
22	M	29	penis 3 months	rash Dec. 2	mucous patches	+	headache +	+ weak	+ +	+
23	F	24	no history	macular 10 days	snail track ulcers	+	headache	–	+ +	+
30	F	50	no history	papulo squamous	nil	+		+	+ +	+

47	F	33	no history	profuse + rupial	mucous patches	+	6 months pregnant	specimen not received	+ +	+
50	M	?	gonorrhoea July, 1917 no sore seen	papular Nov. 17	nil	+		+ weak	+ +	+
67	F	25	vulva 15 weeks	rash 5 days	mucous patches lips	+		+	+ +	+
69	F	23	no history	papulo squamous Dec. 1	nil	+		+	+ +	+
74	F	20	no history	general papular	ulcers	+	had had one dose luargol 0·15	+	+ +	+
79	M	44	penis June, 1917	Syphilitic iritis	Syphilitic iritis		N.A.B. 0·6 one week before	+	+ +	+
84	F	20	no history	general + condylomata	ulcers	+		+	+ +	+
88	M	23	penis 9 months	papular general	mucous patches mouth	+	hair falling +	+	+ +	+
89	M	35	none seen, discharge 1 year	nil	painful tongue mucous patches	+	'peeled' tongue	+	+ +	+
94 A	F	26	labium 6 weeks	nil	snail track ulcers	+		+	+ +	+

TABLE IV. SYPHILIS, GENERALIZED (SECONDARY) TREATED. 11 CASES.

Research No.	*Sex*	*Age*	*Site and date primary*	*Skin*	*Throat*	*Glands*	*W. R. before treatment*	*Treatment*	*Dr. Browning*	*Col. Harrison*	*Dr. McIntosh*
2	M	28	penis 4 years	rash	+	+	+ Dec. 5, 1917	In Belgium. 15 Hg. intramuscular. German Hospital. 1917. 5 Hg. intramuscular. 1917. Galyl 0·3, 0·4, 0·4 and 6 Hg.	–	+ +	+
14	M	25	penis 3 years	rash	+	+	+ July 25, 1917	1915. Three injections, '·606' and 7 Hg. at Lock Hospital. 1917, Aug.–Sept. N.A.B. 0·6, 0·9, 0·9 and 8 Hg.	+ weak	+ +	+
25	M	28	healed chancre 1917 penis	lenticular	+	+	+ August, 1917	1917, Aug.–Sept. Luargol 0·15, 0·15, 0·3 and 8 Hg.	– suspicious	+ +	+
26	M	34	penis May, 1917	papular	+	+	+	1917. N.A.B. 0·6, 0·9, 0·9 and 8 Hg. last Sept.	+	+ +	+
34	M	43	penis Oct. 1914	general	+	+	+ October, 1916	1916, July. Galyl 0·3, 0·4, 0·4 and 8 Hg. 1917, Jan.–March. 8 Hg. 1917, July–Aug. Galyl 0·3, 0·4. 0·4 and Hg. 8	–	–	–
51	F	27	no history	rash	+	+	+ Oct. 3, 1917	1917, April–June. Galyl 0·3, 0·4, 0·4. N.A.B. 0·6. 12 Hg.	suspicious	±	–
52	F	26	no history	rash	+	+	+ Oct. 3, 1917	1917, Oct.–Dec. Galyl 0·3, 0·4, 0·4. 8 Hg.	suspicious	–	–
86	F	17	vulva Nov. 17	macular	nil	+	+ Oct. 31, 1917	1917, Oct.–Dec. Galyl 0·3, 0·4, 0·4. 8 Hg.	–	–	–
94	M	23	penis Oct. 17	papular	+	+	?	1917 Dec.–1918 Jan. 0·3, 0·4, 0·4, 0·4. 8 Hg.	–	±	–
103	F	23	no history	papulo squamous	+	+	+ July 25, 1917	1917 Dec.–1918 Jan. 0·3, 0·4, 0·4, 0·4. 8 Hg.	+	+	+
45	M	37	18 years	18 years ago			?	Definite history, patient a soldier treated by private doctor.	–	–	–

TABLE V. SYPHILIS, LATE (TERTIARY) UNTREATED. 7 CASES.

Research No.	*Sex*	*Age*	*Date primary*	*Nature of Lesions*	*Dr. Browning*	*Col. Harrison*	*Dr. McIntosh*
4	F	32	?	Gummatous ulcer of leg, verified by microscope (Dr. Turnbull); old pelvic cellulitis.	+	+ +	+
35	M	34	?	Gumma of palate, nasal septum destroyed, soft palate partially destroyed.	+	+ +	+
37	M	45	?	Gumma of testis.	+	+ +	+
53	F	39	?	Gumma of ankle. 7 children, 2 pairs of twins, no miscarriage.	+	+ +	+ trace of haemolysis
68	F	39	?	Gummatous ulcer of knee. 13 children, 7 alive, 2 miscarriages, 1 still birth.	+	+ +	+
83	M	30	?	Extensive ulceration of fauces with much loss of tissue. Also had diphtheria—Klebs Loeffler B. found	+	+ +	+
92	F	30	?	Gummatous ulcer of right leg 6 weeks. Impetigo-like eruption of scalp 3 months.	+	+ +	+

TABLE VI. SYPHILIS, LATE NERVOUS.

Research No.	*Sex*	*Age*	*Date primary*	*Nature of Lesions*	*Dr. Browning*	*Col. Harrison*	*Dr. McIntosh*
80	M	43	?	Left hemiplegia 3 weeks before. K. J. + + Spastic gait. Scars of gummata on legs. No regular treatment.	–	+ ±	+

TABLE VII. SYPHILIS, LATE (TERTIARY) TREATED. 7 CASES.

Research No.	*Sex*	*Age*	*Site and date, primary*	*Lesions*	*W. R. before treatment*	*Treatment*	*Dr. Browning*	*Col. Harrison*	*Dr. McIntosh*
8	M	30	penis 8 years	Gummatous ulcers, throat	+	N.A.B. 0·6, 0·9, 0·9. 8 Hg. Aug.–Sept. 1917.	–	±	+
17	F	36	?	Old ulcer, mouth, nose, palate scarred. 2 miscarriages. one girl W. R. +	+	Mercury and iodides internally. No '606'.	–	+ +	+
18	F	36	?	Large healed gummatous ulcer inner canthus involving orbit and nose.	+	1915. 3 injections, Galyl 0·3, 0·4, 0·4. Hg. internally + KI for 2 years.	–	–	+ incomplete
54	F	22	?	Gumma of foot.	?	4 intravenous injections given at infirmary 4 months ago.	+	+ +	specimen damaged
58	M	40	penis 14 years	Gummatous ulcers of legs.	+ Aug. 1916	1916. 0·3, 0·4, 0·4 Galyl. Hg. and KI internally to Dec. 1917	suspicious	±	–
76	M	40	?	An old case, had much internal treatment for 15 years.	+	Dec. 1917. Jan. 1918. N.A.B. 0·6, 0·9, 0·9. 8 Hg.	+	+ ±	+
91	F	35	?	Gummata loin and right ear.	March 21, 1917 + Jan. 2, 1918 +	March–April, 1917. NAB. 0·6, 0·75, 0·9. 8 Hg. Hg. and KI internally to Sept. 1917.	–	–	–

TABLE VIII. SYPHILIS: LATENT. 3 CASES.

Research No.	*Sex*	*Age*	*Reasons for examination*	*Dr. Browning*	*Col. Harrison*	*Dr. McIntosh*
5	F	32	Mother of a congenital syphilitic infant. The infant had a rash on buttocks, legs, and neck. Spleen +. Three healthy children and two miscarriages since.	+	+ +	+
62	M	34	Sent by surgeon who was treating haemorrhoids, because there was a history of a rash one year before. Glands +, *no* condylomata, throat unaffected.	+ weak	+ +	+
75	M	50	Wife and child W. R. + Patient has no symptoms and gives no history pointing to syphilis.	+	+ +	+

TABLE IX. SYPHILIS, HEREDITARY (CONGENITAL). 3 CASES.

Research No.	*Sex*	*Age*	*Symptoms*	*Dr. Browning*	*Col. Harrison*	*Dr. McIntosh*
56	F	14	Complete deafness. Hutchinson's teeth. Interstitial keratitis. Perforation of nasal septum ozaena. (W. R. + previously, McIntosh.)	+	+ +	Specimen damaged
81	F	9	Hutchinson's teeth. Perforation of hard palate. Depressed nose. Ulceration of nasal cavity, ozaena.	+	+ +	+
93	F	13	Old interstitial keratitis. Deaf. Teeth *not* characteristic.	+	+	+

TABLE X. CASES SENT FOR DIAGNOSIS. 3 CASES.

Research No.	*Sex*	*Age*	*Reasons for examination*	*Dr. Browning*	*Col. Harrison*	*Dr. McIntosh*
27	M	65	Seven months ago 'sores' on the body. One epitrochlear gland + sent to clinic as ? syphilis.	Broken in transit	–	–
28	F	31	Her married sister, with whom she was sleeping, treated at London Hospital for secondary syphilis, condylomata, &c. The patient had sores on her feet (? scabies) 14 days before. W. R. – trace (Dr. McIntosh) on Jan. 30, 1918, no treatment.	–	±	– Feb. 11, 1918
48	M	35	A soldier, husband of No. 47, who had a profuse secondary rash. This man is said to have had a 'soft' sore three months before. W. R. –. He went back to France the day after his blood was examined. The wife was 6 months pregnant. Vide Table III, p. 34.	–	–	–

In Nos. 40, 63, 70, 77 and 85 syphilis has been suspected or diagnosed elsewhere on account of miscarriages, &c. They are included in Table XI.

TABLE XI. NON-SYPHILITIC CASES, CLASSIFIED. 25 CASES.

Research No.	*Sex*	*Age*	*Nature of illness*	*Dr. Browning*	*Col. Harrison*	*Dr. McIntosh*
13	M	20	Ulcus molle, foreskin 3 weeks appearing 7 days after coitus, glands *not* indurated, no treatment.	–	–	–
2	M	28	Lupus vulgaris (exulcerans) 4 years. Nose affected.	+*	–	–
46	M	22	Lupus vulgaris 4 years. Operation for tuberculous glands at West London Hospital. Chest, face, neck, and shoulders affected.	–	–	–
61	M	21	Lupus vulgaris since early childhood. Nose affected + + ulceration.	–	–	–
90	F	41	Lupus vulgaris, 10 years extensive ulceration of nose with destruction of cartilaginous septum.	not examined	–	–
98	M	15	Lupus vulgaris 11 years. Both sides of face affected. Nose ulcerated. Glands of neck +.	–	–	–
43	M	32	Tuberculous ulcer of lower lip. Gland +. Advanced pulmonary tuberculosis (Dr. Cecil Wall), direct infection of lip by sputum. So called 'Tuberculosis cutis orificialis'.	–	–	–
32	F	34	Lupus erythematosus, acute outbreak in a chronic case. Rigors. T. 104·2°. Blood taken next day. Eruption face and hands.	–	–	–
55	F	40	Lupus erythematosus. Old tuberculous glands of neck. Breast removed for tuberculosis, May 1917. Eruption on cheeks, ears, &c. Alopecia.	–	–	–
82	F	32	Lupus erythematosus in a deaf-mute. Chronic type 9 years' duration.	–	–	–
57	M	50	Leprosy, contracted in the East. Maculo-anaesthetic type, 10 years. Ulnar thickening, atrophy of interossii. Hansen's bacilli found. No history or sign of syphilis.	–	± see note (*a*) at foot	–
64	F	55	Leprosy, contracted in Odessa, at least 12 years' duration. Nodular type. Hansen's bacilli demonstrated in sections.	–	–	–

* *See note, p. 48.*

TABLE XI. NON-SYPHILITIC CASES, CLASSIFIED (*cont.*).

Research No.	*Sex*	*Age*	*Nature of illness*	*Dr. Browning*	*Col. Harrison*	*Dr. McIntosh*
71	F	18	Scleroderma, Morphoea band type, left arm and fore-arm. No history or evidence of syphilis.	—	+ see note (*b*) at foot	— trace
21	M	20	Scabies. One epitrochlear gland +.	—	—	—
77	M	26	Scabies. Sore throat suspicious of syphilis, epitrochlear glands + + no history of chancre. No treatment. Syphilis + scabies was suspected by J. H. Sequeira.	—	—	—
24	M	8	Psoriasis—characteristic case.	—	—	—
31	F	39	Seborrhoide, scalp and back affected. Itching.	—	—	—
39	M	22	Seborrhoide, chest-flexors and back affected. Itching.	—	—	—
40	F	52	Tinea, eczema marginatum eczematoid ringworm of the feet, mycelium found in the scales by J. H. Sequeira. This case had been diagnosed as syphilis at another hospital, and a + reaction reported.	—	—	—
70	F	26	Erythema of the palms with swollen joints, probably rheumatoid arthritis. 1 child died at birth. W. R. taken to exclude syphilis.	—	—	—
63	F	40	Furunculosis and carbuncle. No sugar. History of 4 miscarriages and 4 children died in infancy out of 9.	—	—	—
99	M	36	Carbuncles. Ill one week. No sugar. Had had one dose of vaccine 6 hours before blood was taken.	+	+ ± see note (*c*) at foot	—
97	M	12	Diabetes. Greatly wasted child passing a large quantity of sugar.	—	—	—
101	M	53	Diabetic gangrene. Diabetes at least 2 years. Amputation of right leg. T. 103°.	—	—	—
85	F	35	Graves' disease. Thyroid + +, exophthalmos, tachycardia. 1 living child, 5 miscarriages.	—	—	—

TABLE XI. NON-SYPHILITIC CASES, CLASSIFIED (*cont.*).

Research No.	*Sex*	*Age*	*Nature of illness*	*Dr. Browning*	*Col. Harrison*	*Dr. McIntosh*
38	M	21	Follicular tonsillitis. Streptococcal (Dr. Panton).	—	—	—
95 A	F	14	Acute rheumatism T. 101°. F. Heart free, elbows and knees affected. Profuse sweating.	—	—	—
96	M	?	Ulcerative endocarditis. T. 103° to 104°. Mitral systolic murmur. Septic appearance. The blood clotted at once on removal.	—	—	—
100	M	16	Osteomyelitis of femur, 3 months' duration. Septic temperature.	—	—	—
102	M	11	Osteomyelitis of femur, 3 months' duration. Septic temperature.	— suspicious	±	—

(*a*) Leprosy sometimes gives a positive reaction. In my experience of 14 cases, the reaction was always negative in maculo-anaesthetic cases, and it is generally recognized as being commoner in the nodular variety.

(*b*) Scleroderma has been reported by other observers as giving a positive reaction. In four of my cases it was negative.

(*c*) This patient had had an injection of vaccine six hours before blood was taken. I do not think this is of moment, but put it on record. [The Committee call attention to the fact that in this case a positive result was obtained in Dr. Browning's laboratory, at Rochester Row, and by Dr. Donald (see Table XIV), who tested the same sample of serum as did Dr. McIntosh. Col. Harrison informs the Committee that the reaction obtained in his laboratory was confirmed in the second tube. A further sample of this blood, obtained by Dr. McIntosh at a later date, on being tested gave a positive reaction in his hands also. On serological evidence it would appear therefore that this case was one of latent syphilis.]

TABLE XII. ANALYSIS OF RESULTS IN SYPHILITIC CASES.

A. UNTREATED CASES.

	Dr. Browning	*Col. Harrison*	*Dr. McIntosh*
Primary. 15 cases			
Positive	11	11	11
Suspicious	2	1	1
Negative	2	3	2
No return	0	0	1
	15	15	15
Secondary. 20 cases			
Positive	17 (2 weak)	20	20
Suspicious	0	0	0
Negative	2	0	0
No return	1	0	0
	20	20	20
Tertiary and *late Nervous.* 8 cases			
Positive	7	8	8
Suspicious	0	0	0
Negative	1	0	0
No return	0	0	0
	8	8	8
Latent. 3 cases			
Positive	3 (1 weak)	3	3
Suspicious	0	0	0
Negative	0	0	0
No return	0	0	0
	3	3	3
Hereditary. 3 cases			
Positive	3	3	2
Suspicious	0	0	0
Negative	0	0	0
No return	0	0	1
	3	3	3

B. TREATED CASES.

	Dr. Browning	*Col. Harrison*	*Dr. McIntosh*
Primary. 4 cases. W. R. + before treatment			
Positive	0	0	0
Suspicious	0	0	0
Negative	4	4	4
No return	0	0	0
	4	4	4
Secondary. 11 cases			
Positive	3 (1 weak)	5	5
Suspicious	3	2	0
Negative	5	4	6
No return	0	0	0
	11	11	11
Tertiary. 7 cases			
Positive	2	3	4 (1 incomplete)
Suspicious	1	2	0
Negative	4	2	2
No return	0	0	1
	7	7	7

TABLE XIII. SUMMARY OF RESULTS.

A. Untreated cases of syphilis — 49

	Dr. Browning	*Col. Harrison*	*Dr. McIntosh*
Positive	41 (3 weak)	45	44 (1 incomplete)
Suspicious	2	1	1
Negative	5	3	2
No return	1	0	2
	49	49	49

B. Treated cases of syphilis — 22

	Dr. Browning	*Col. Harrison*	*Dr. McIntosh*
Positive	5 (1 weak)	8	9 (1 incomplete)
Suspicious	4	4	0
Negative	13	10	12
No return	0	0	1
	22	22	22

C. Cases sent for 'diagnosis' — 3

	Dr. Browning	*Col. Harrison*	*Dr. McIntosh*
Positive	0	0	0
Suspicious	0	1	0
Negative	2	2	3
No return	1	0	0
	3	3	3

D. Cases with no clinical evidence of syphilis — 30

	Dr. Browning	*Col. Harrison*	*Dr. McIntosh*
Positive	2	2	0
Suspicious	1	2	1 (trace)
Negative	26	26	29
No return	1	0	0
	30	30	30

The detailed comparison of the results returned by the three observers is instructive. To make this perfectly fair I have excluded those cases in which one or other observer failed to make returns. These failures were due to non-receipt or breakage of specimens, or some doubt as to proper numbering.

(*a*) *Comparison of Dr. Browning's with Colonel Harrison's results.*

101 cases were compared.
In 84 cases the results were identical.
In 10 cases the differences on the returns were important:

Syphilitic Cases	*Browning*	*Harrison*	*Diagnosis*
No. 7	+	±	Primary
66	−	+ +	Primary untreated
12	−	+ +	Secondary treated
17	−	+ +	Tertiary treated
19	−	+ +	Secondary untreated
23	−	+ +	Secondary untreated
25	− suspicious	+ +	Secondary treated
80	−	+ ±	Tertiary untreated
Non-syphilitic Cases			
2	+	−	Lupus
71	−	+	Scleroderma

Minor differences were as follows:

	Browning	*Harrison*	
Case 8	—	$\underline{\pm}$	Tertiary treated
,, 10	suspicious	—	Primary untreated
,, 16	very suspicious	—	Primary untreated
,, 28	—	±	For Diagnosis
,, 52	suspicious	—	Secondary treated
,, 94	—	±	Secondary treated
,, 57	—	$\underline{\pm}$	Leprosy

(b) *Comparison of Dr. Browning's with Dr. McIntosh's results.*

98 cases were compared, no returns having been made from each of these gentlemen in three cases.

81 results were identical.

In 11 cases the difference in the returns was important:

Syphilitic Cases	*Browning*	*McIntosh*	
8	—	+	Tertiary treated
12	—	+	Secondary treated
17	—	+	Tertiary treated
18	—	+ incomplete	Tertiary treated
19	—	+	Secondary untreated
23	—	+	Secondary untreated
25	— suspicious	+	Secondary treated
66	—	+	Primary untreated
80	—	+	Tertiary untreated
Non-syphilitic Cases			
2	+	—	Lupus
99	+	—	Carbuncles

Minor variations were as follows:

16	very suspicious	—	Primary untreated
51	suspicious	—	Secondary treated
52	suspicious	—	Secondary treated
58	suspicious	—	Tertiary treated
71	—	— trace	Non-syphilitic
102	— suspicious	—	Non-syphilitic

(c) *Comparison of Colonel Harrison's with Dr. McIntosh's results.*

101 cases were compared.

90 results were identical.

In no syphilitic cases were the differences serious, the only marked variation was in the following non-syphilitic case.[1]

	Harrison	*McIntosh*	
Case 99	+ ±	—	Carbuncles

Minor variations were as follows:

Case 8	±	+	Tertiary treated
,, 18	—	+ incomplete	Tertiary treated
,, 51	±	—	Treated case
,, 58	$\underline{\pm}$	—	Tertiary treated
,, 94	±	—	Secondary treated
,, 71	+	— trace	Scleroderma
,, 102	±	—	Osteomyelitis
,, 10	—	— trace	Primary untreated
,, 28	±	—	Sores on feet, sent for diagnosis
,, 57	$\underline{\pm}$	—	Leprosy

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[1] See note (*c*), p. 43.

§ 5. *Conclusions.*

(1) The techniques of Colonel Harrison and Dr. McIntosh give remarkably close results, the only important divergence being in a case of carbuncles (clinically non-syphilitic) which Colonel Harrison returned as + ± and Dr. McIntosh as negative. Dr. Browning returned the same case as +.

In three syphilitic cases (all treated) Dr. McIntosh's technique appeared more sensitive than that of Colonel Harrison:

		Harrison	*McIntosh*	
Case	8	±	+	Tertiary treated
,,	18	—	+ incomplete	Tertiary treated
,,	10	—	— trace	Primary untreated

while in three other syphilitic cases (all treated) Colonel Harrison's reaction suggests a greater sensibility than that of Dr. McIntosh:

Case	51	±	—
,,	58	±	—
,,	94	±	—

Colonel Harrison's results also showed a + reaction in (71) a case of scleroderma (McIntosh – trace, Browning –), and a ± in (102) a case of osteomyelitis with fever (McIntosh – (suspicious), Browning –).

(2) Dr. Browning's results compared with the other two observers are not so close and differ from the clinical diagnosis in several instances:

	Browning	*Harrison*	*McIntosh*
Primary untreated syphilis			
No. 7	+	±	No return
* ,, 66	—	+ +	+
Secondary untreated syphilis			
*No. 19	—	+ +	+
,, 22	+ weak	+ +	+
* ,, 23	—	+ +	+
Secondary treated syphilis			
*No. 12	—	+ +	+
* ,, 14	+ weak	+ +	+
* ,, 25	— suspicious	+ +	+
Tertiary treated syphilis			
*No. 17	—	+ +	+
Lupus vulgaris			
*No. 2	+	—	—

Those marked with * are important clinically, and five of the eight occurred in one batch of specimens, the blood being taken on February 7, 1918.[1] The other differences were negligible. Nos. 10 and 16 (primary untreated) were returned ‘suspicious’ and ‘very suspicious’ when Colonel Harrison gave negative reports, and Dr. McIntosh returned them respectively as ‘negative, trace’ and ‘positive incomplete’.

(3) It would be an advantage, if a standardized technique be introduced, to insist on a standard system of returns, which for the purposes of the general practitioner should, I think, be as simple as possible and in a qualitative rather than a quantitative sense. The practitioner wants to know, (*a*) if untreated, whether his patient is syphilitic or not, i. e. whether anti-syphilitic treatment is or is not required; (*b*) in a treated case, whether he is to continue treatment. Quantitative reports would, of course, be of value in the venereal clinics, especially for the comparison of the methods of treatment.

Dr. Browning desires it to be known that Dr. E. L. Kennaway was associated with him in the observations recorded in this research.

I should like to acknowledge my indebtedness to my clinical assistant, Dr. Vilvandré, who has given me valuable help in taking the specimens of blood, and in the notes of the cases, and to my colleagues at the London Hospital for placing at my disposal ten medical and surgical cases.

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[1] The Committee think it fair to Dr. Browning to state their opinion that the value of his method should not be judged by these five divergent results. It is probable that some defect existed in his technique on one particular day, for the sera from the same cases were subsequently retested in his laboratory with results substantially coinciding with those reached by the other observers.

Further, in the case of one apparently erroneous result sent in by Dr. Browning (viz. No. 2, *Lupus vulgaris*) the laboratory records were found to show that his actual result was negative, and not positive as appears in Dr. Sequeira’s Table XI and following summaries. The Committee have satisfied themselves that in this instance the wrong return was due to a simple clerical error on Dr. Browning’s part. They would draw attention to this example of the readiness with which clerical errors may contribute to the apparent uncertainties of the test.

III

TABULAR SUMMARY OF THE RESULTS

III.

TABLE XIV. TABULAR SUMMARY OF THE RESULTS.

Research No.	*Sex*	*Age*	*Clinical diagnosis*	*Dr. Browning*	*Col. Harrison*	*Dr. McIntosh*	*Dr. Donald (see p. 4)*
1	M	26	Secondary syphilis: untreated	+	+ +	+	+
2	M	28	Lupus vulgaris	+	—	—	—
3	F	22	Secondary syphilis: untreated	+	+ +	+	+
4	F	32	Tertiary syphilis: untreated	+	+ +	+	+
5	F	32	Latent syphilis	+	+ +	+	+
6	F	37	Secondary syphilis: untreated	+	+ +	+	+
7	M	53	Primary syphilis, penis. 18 days	+	±	test unsatisfactory	test and control had each about 20 % haemolysis
8	M	30	Tertiary syphilis: treated	—	±	+	pos. incomplete
9	M	29	Secondary syphilis: untreated	+	+ +	+	not tested
10	M	30	Primary syphilis, penis. 1 week	suspicious	—	neg. trace	partially +
11	M	29	Secondary syphilis: untreated	+	+ +	+	+
12	M	28	Secondary syphilis: treated	—	+ +	+	+
13	M	20	Ulcus molle	—	—	—	—
14	M	25	Secondary syphilis: treated	+ (weak)	+ +	+	+
15	M	21	Secondary syphilis: untreated	+	+ +	+	+
16	F	21	Primary syphilis, lower lip. 2 weeks	very suspicious	—	—	neg. incomplete
17	F	36	Tertiary syphilis: treated	—	+ +	+	+
18	F	36	Tertiary syphilis: treated	—	—	+ (incomplete)	+ incomplete
19	M	30	Secondary syphilis: untreated	—	+ +	+	+
20	M	42	Primary syphilis, penis: untreated	+	+ +	+	+
21	M	20	Scabies	—	—	—	—
22	M	29	Secondary syphilis: untreated	+ (weak)	+ +	+	+
23	F	24	Secondary syphilis: untreated	—	+ +	+	+
24	M	8	Psoriasis	—	—	—	—
25	M	28	Secondary syphilis: treated	— suspicious	+ +	+	+

26	M	34	Secondary syphilis: treated	+	+ +	+	+
27	M	65	Sores on body 7 months ago. Syph.?	not examined	—	—	—
28	F	31	Sores on feet	—	±	—	—
29	M	29	Primary syphilis, penis: untreated	—	—	—	—
30	F	50	Secondary syphilis: untreated	+	+ +	+	+
31	F	39	Seborrhoide—not syphilitic	—	—	—	—
32	F	32	Lupus erythematosus	—	—	—	—
33	M	31	Primary syphilis: treated	—	—	—	—
34	M	43	Secondary syphilis: treated	—	—	—	—
35	M	34	Tertiary syphilis: untreated	+	+ +	+	+
36	M	20	Primary syphilis, penis: untreated	+	+ +	+	+
37	M	45	Tertiary syphilis: untreated	+	+ +	+	+
38	M	21	Follicular tonsillitis	—	—	—	—
39	M	22	Seborrhoide—not syphilitic	—	—	—	—
40	F	52	Eczema marginatum	—	—	—	—
41	F	?	Primary syphilis: treated	—	—	—	—
42	F	22	Primary syphilis, labium; untreated	+	+ +	+	+
43	M	32	Tuberculous ulcer of lip; phthisis	—	—	—	—
44	M	38	Primary syphilis, penis; untreated	+	+ +	+ (incomplete)	+
45	M	37	Secondary syphilis: treated	—	—	—	— incomplete
46	M	22	Lupus vulgaris	—	—	—	—
47	F	33	Secondary syphilis: untreated	not examined	+ +	+	+
48	M	35	Husband of No. 47. 'Soft sore' 3 months ago	—	—	—	—
49	F	22	Primary syphilis, vulva: untreated	+	+ +	+	+
50	M	?	Secondary syphilis: untreated	+ (weak)	+ +	+	+
51	F	27	Secondary syphilis: treated	suspicious	±	—	—
52	F	26	Secondary syphilis: treated	suspicious	—	—	—
53	F	39	Tertiary syphilis: untreated	+	+ +	+	+
54	F	22	Tertiary syphilis: treated	+	+ +	tr. of haemol. not examined	not examined
55	F	40	Lupus erythematosus	—	—	—	—
56	F	14	Congenital syphilis	+	+ +	not examined	not examined
57	M	50	Lepra maculo-anaesthetica	—	±	—	—
58	M	40	Tertiary syphilis: treated	suspicious	±	—	—

TABLE XIV. TABULAR SUMMARY OF THE RESULTS (*continued*).

Research No.	*Sex*	*Age*	*Clinical diagnosis*	*Dr. Browning*	*Col. Harrison*	*Dr. McIntosh*	*Dr. Donald*
59	M	26	Primary syphilis: treated	—	—	—	—
60	M	21	Primary syphilis: untreated	+	+ +	+	+
61	M	21	Lupus vulgaris	—	—	—	—
62	M	34	History of rash 1 year ago. Glands +	+ (weak)	+ +	+	+
63	F	40	Furunculosis and carbuncle	—	—	—	—
64	F	55	Lepra tuberosa	—	—	—	—
65	F	22	Primary syphilis: untreated	+	+ +	+	+
66	M	22	Primary syphilis: untreated	—	+ +	+	not examined
67	F	25	Secondary syphilis: untreated	+	+ +	+	+
68	F	39	Tertiary syphilis: untreated	+	+ +	+	+
69	F	23	Secondary syphilis: untreated	+	+ +	+	+
70	F	26	Erythema of palms	—	—	—	—
71	F	18	Scleroderma—morphoea	—	+	— trace	—
72	M	23	Primary syphilis: untreated	+	+ +	+	+
73	M	20	Primary syphilis: untreated	+	+ +	+	+
74	F	20	Secondary syphilis: untreated	+	+ +	+	+
75	M	50	Latent syphilis. Wife and child W. R +	+	+ +	+	+
76	M	40	Tertiary syphilis: treated	+	+ ±	+	+
77	M	26	Scabies, sore throat	—	—	—	—
78	M	23	Primary syphilis: untreated	+	+ +	+	+
79	M	44	Secondary syphilis: untreated	+	+ +	+	+
80	M	43	Tertiary syphilis: untreated	—	+ ±	+	+
81	F	9	Congenital syphilis	+	+ +	+	+
82	F	32	Lupus erythematosus	—	—	—	—
83	M	30	Tertiary syphilis: untreated	+	+ +	+	+
84	F	20	Secondary syphilis: untreated	+	+ +	+	+
85	F	35	Graves' disease	—	—	—	—
86	F	17	Secondary syphilis: treated	—	—	—	—
87	F	20	Primary syphilis: treated	—	—	—	—
88	M	23	Secondary syphilis: untreated	+	+ +	+	+
89	M	35	Secondary syphilis: untreated	+	+ +	+	+

90	F	41	Lupus vulgaris	not examined	—	—	—
91	F	35	Tertiary syphilis : treated	—	—	—	—
92	F	30	Tertiary syphilis : untreated	+	+ +	+	+
93	F	13	Congenital syphilis	+	+	+	+
94	M	23	Secondary syphilis : treated	—	±	—	—
94 A	F	26	Secondary syphilis : untreated	+	+ +	+	+
95 A	F	14	Acute rheumatism	—	—	—	—
96	M	?	Ulcerative endocarditis	—	—	—	—
97	M	12	Diabetes	—	—	—	—
98	M	15	Lupus vulgaris	—	—	—	—
*99	M	36	Carbuncles	+	+ ±	—	+
100	M	16	Osteomyelitis of femur	—	—	—	—
101	M	53	Diabetic gangrene	—	—	—	—
102	M	11	Osteomyelitis of femur	— (suspicious)	±	—	—
103	F	23	Secondary syphilis : treated	+	+	+	+

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* See note (*c*), p. 43.

IV. CONCLUSIONS OF THE COMMITTEE

The Committee have thought it right, in presenting Dr. Sequeira's report, to publish the original returns sent in by each observer as they stood. Where errors were subsequently discovered, they have been indicated in foot-notes, and it is noteworthy that if account be taken of these the evidence as to the accuracy of the test itself is strengthened. In other words, Dr. Sequeira's summaries exaggerate the margin of mistakes actually committed in the testing.

Upon the study of all the observations presented in this Report, the Committee consider that in the hands of those whose previous record entitles them to be considered as experts, the percentage of positive Wassermann reactions in active syphilis is so high that the test may, for all practical purposes, be looked upon as specific. It must not be forgotten that the performance of the Wassermann test involves one of the most complicated methods that have been applied to diagnosis in medicine, a fact which has already been emphasized by the Committee in their former report upon its technique. Practised as it has been by all sorts of laboratory workers, it was only to be anticipated that in some instances at least inaccurate or fallacious results should have been obtained. Such failures have in certain quarters led to a scepticism with regard to the results, or even to the value of the method itself. Much of the criticism and scepticism, however, has been based on mere statement, and a searching inquiry into the literature of the last eight years reveals, in the opinion of the Committee, really very little that can be classed as proved inaccuracy. There is, indeed, a much greater volume of published evidence in favour of the Wassermann test.

It cannot be expected that this, or indeed any similar biological test, should invariably reveal the presence of some particular disease. The diagnostic value of any such test may be impaired either by the imperfection of the test itself, or by some failure in its performance, or by idiosyncrasy of the patient, whereby he may fail to react characteristically.

The Committee had these points in mind when they undertook the fresh investigation which has been given above. While the number of cases in this is small compared with that in some of the published series referred to, the Committee can claim that the work has been done as carefully and as objectively as possible by all concerned, and it is now recorded with a wealth of detail which has not been provided in any similar publication. From the records given here it is believed that any intelligent reader will be able to form his own opinion of the clinical value of the Wassermann reaction.

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